# Background Information for the

# October 2002 ACPS Meeting

# Scientific Considerations of Polymorphism in Pharmaceutical Solids: Abbreviated New Drug Applications

## INTRODUCTION

Many pharmaceutical solids can exist in different physical forms. Polymorphism is often characterized as the ability of a drug substance to exist as two or more crystalline phases that have different arrangements and/or conformations of the molecules in the crystal lattice (1). Amorphous solids consist of disordered arrangements of molecules and do not possess a distinguishable crystal lattice. **Solvates** are crystalline solid adducts containing either stoichiometric or nonstoichiometric amounts of a solvent incorporated within the crystal structure. If the incorporated solvent is water, the **solvates** are also commonly known as hydrates. Polymorphism refers to the occurrence of different crystalline forms of the same drug substance. Polymorphism in this commentary is defined as in the International Conference on Harmonization (ICH) Guideline Q6A (2), to include solvation products and amorphous forms.

Polymorphs and/or **solvates** of a pharmaceutical solid can have different chemical and physical properties such as melting point, chemical reactivity, apparent solubility, dissolution rate, optical and electrical properties, vapor pressure, and density. These properties can a direct impact on the process-ability of drug substances and the quality/performance of drug products, such as stability, dissolution, and bioavailability. A metastable pharmaceutical solid form can change crystalline structure or solvate/desolvate in response to changes in environmental conditions, processing, or over time.

Several regulatory documents and literature reports (2-4) address issues relevant to the regulation of polymorphism. The concepts and principles outlined in these are applicable for an ANDA. However, certain additional considerations may be applicable in case of ANDAs. Often at the time FDA receives an ANDA a monograph defining certain key attributes of the drug substance and drug product may be available in the Unites States Pharmacopoeia (USP). These public standards play a significant role in the ANDA regulatory review process and in case of polymorphism, when some differences are noted, lead to additional requirements and considerations. This commentary is intended to provide a perspective on polymorphism in pharmaceutical solid in the context of ANDAs. It highlights major considerations for monitoring and controlling drug substance polymorphs and describes a framework for regulatory decisions regarding drug substance "sameness" considering the role and impact of polymorphism in pharmaceutical solids.

## POLYMORPHISM IN PHARMACEUITCAL SOLID DRUG SUBSTANCE AND THE ISSUE OF "SAMENESS"

FDA may refuse to approve an ANDA referencing a listed drug if the application contains insufficient information to

show that the drug substance is the "same" as that of the reference listed drug. A drug substance in a generic drug product is generally considered to be the same as the drug substance in the reference listed drug if it meets the same standards for identity. In most cases, the standards for identity are described in the USP although FDA may prescribe additional standards when necessary. Because drug product performance depends on the product formulation, the drug substance in a proposed generic drug product need not have the same physical form (particle size, shape, or polymorph form) as the drug substance in the reference listed drug. An ANDA applicant is required to demonstrate that the proposed product meets the standards for identity, exhibits sufficient stability and is bioequivalent to the reference listed drug.

Over the years FDA has approved many generic drug products based upon a drug substance with different physical form from that of the drug substance in the respective reference listed drug (e.g., warfarin sodium, famotidine, and ranitidine). Also many ANDAs have been approved in which the drug substances differed from those in the corresponding reference listed drugs with respect to solvation or hydration state (e.g., terazosin hydrochloride, ampicillin, and cefadroxil).

Since polymorphs exhibit certain differences in physical (e.g., powder flow and compactability, apparent solubility and dissolution rate) and solid state chemistry (reactivity) attributes that relate to stability and bioavailability it is essential that the product development and the FDA review process pay close attention to this issue. This scrutiny is essential to ensure that polymorphic differences (when present) are addressed via design and control of formulation and process conditions to physical and chemical stability of the product over the intended shelf-life, and bioavailability/bioequivalence.

## CHARACTERIZATION OF POLYMORPHS

A number of methods have been employed for characterizing polymorphs in pharmaceutical solids (5). Polarizing optical microscopy and thermomicroscopy have proven to be useful tools. Thermal analysis procedures, such as differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA), can be used to obtain additional information, including phase changes, and to deduce whether each isolated form is a solvate or anhydrate. These thermal methodologies are employed to distinguish between enantiotropic and monotropic systems. For an enantiotropic system, the relative stability of a pair of solid forms inverts at some transition temperature beneath the melting point while a single form is always more stable beneath the melting point in a monotropic system (5).

The utility of solid-state spectroscopy for characterization of polymorphic systems is becoming exceedingly important. Nuclear magnetic resonance (NMR), infrared absorption, and Raman spectroscopy are used to study crystal structures. These methods require that either the nuclei of the pair of substances being examined exist in magnetically inequivalent environments or the vibrational modes are sufficiently different between the structural forms to permit differentiation.

It should be emphasized that the definitive criterion for the existence of polymorphism is via demonstration of a nonequivalent crystal structure, usually by comparison of the x-ray diffraction patterns. Microscopy, thermal analysis methodology, and solid state NMR are generally considered as sources of supporting information.

## PROPERTIES OF POLYMORPHS

### Solubility and Dissolution

The solid state characteristics of drugs are known to potentially exert a significant influence on the *solubility parameter*. Polymorphs of a drug substance can have different apparent aqueous solubility and dissolution rate, when such differences are sufficiently large bioavailability is altered and it is often difficult to formulate a bioequivalent drug product using a different polymorph.

Solubility at a defined temperature and pressure is the saturation concentration of the dissolved drug in equilibrium with the solid drug. Aqueous solubility of drugs is traditionally determined using the equilibrium solubility method that

involved suspending an excess amount of a solid drug in a selected aqueous medium. The equilibrium solubility method may not be suitable to determine the solubility of a metastable form, since the metastable form may convert to the stable form during the experiment.

When the solubility of metastable forms of a drug substance can not be determined by the equilibrium method, the intrinsic dissolution method may be useful to deduce the relative solubilities of metastable forms (6). Use of the intrinsic dissolution method assumes that the intrinsic dissolution rate is proportional to the solubility - the proportionality constant being the transport rate constant, which is constant under the same hydrodynamic conditions in a transport-controlled dissolution process.

Polymorphic differences and transformation that result in different apparent solubility and dissolution rate are generally detected by dissolution testing. This test provides a suitable means to identify and control the quality of a product from both bioavailability and (physical) stability perspectives. When solubility and dissolution rate of the relevant polymorph forms are sufficiently high and controlled via dissolution regulatory concerns with respect to bioavailability and stability are minimum. The Biopharmaceutics Classification (7,8) criteria of high solubility and rapid dissolution should be considered in regulatory decisions.

**Stability and Manufacture-ability**

Polymorphs of a pharmaceutical solid may have different physical and solid state chemical (reactivity) properties (9). The most stable polymorphic form of a drug substance is often used because it has the lowest potential for conversion from one polymorphic form to another while the metastable form may be used to enhance the bioavailability. Gibbs free energy, thermodynamic activity, and solubility provide the definitive measures of relative polymorphic stability under defined conditions of temperature and pressure. The relative polymorphic stability may be determined by an iterative examination of the relative apparent solubility of supersaturated solutions of polymorphic pairs. Since the rate of conversion to the more stable form is often rapid when mediated by the solution phase, the less stable polymorph with the greater apparent solubility dissolves, while the more stable polymorph with the lower apparent solubility crystallizes out upon standing.

Solid-state reactions include solid-state phase transformations, dehydration/desolvation processes, and chemical reactions. One polymorph may convert to another during manufacturing and storage, particularly when a metastable form is used. Since an amorphous form is thermodynamically less stable than any crystalline form, inadvertent crystallization from an amorphous drug substance may occur. As a consequence of the higher mobility and ability to interact with moisture, amorphous drug substances are also more likely to undergo solid-state reactions.

In addition, phase conversions of some drug substances are possible when exposed to a range of manufacturing processes (10). Milling/micronization operations may result in polymorphic form conversion of a drug substance. In the case of wet granulation processes, where the usual solvents are aqueous, one may encounter a variety of interconversions between anhydrates and hydrates, or between different hydrates. Spray-drying processes have been shown to produce amorphous drug substances. However, phase conversions should not be of concern if they occur consistently.

**CONSIDERATIONS OF POLYMORPHISM IN ANDAs**

Decision Trees #1 - #3, as shown in Figure 1, provide a process for evaluating when and how polymorphs of drug substances in ANDAs should be monitored and controlled. These decision trees were developed based on the ICH Guideline Q6A decision trees on polymorphism (2) and adopt the concepts from the Biopharmaceutics Classification System (7, 8).

Decision Tree #1 considers whether there is a need to set polymorphic acceptance criteria in drug substances and drug products. If no known polymorphs exist or all known polymorphs are highly soluble and sufficiently stable, it is expected that polymorphism is unlikely to have an effect on bioavailability and stability. This approach assumes that adequate knowledge of drug substance polymorphs is available by the time an ANDA is filed.

Decision Tree #2 discusses how to set a polymorph specification for a drug substance, given the fact that at least one polymorph is known to have low solubility based on the BCS. If an ANDA has the same polymorph specification as the U. S. Pharmacopoeia (USP), and the USP specification is adequate, no further polymorphic test or acceptance criteria for the drug substance beyond the existing USP methodology would be necessary. Otherwise, an ANDA applicant should set a new polymorphic acceptance criterion for the drug substance.

Decision Tree #3 discusses if there is a need to set a polymorph specification for a drug product. It is not necessary to have a polymorph specification for a drug product if the most stable polymorphic form is used or the form is used in a previously approved product(s) that was developed *without extraordinary formulation or manufacturing process development effort*. Furthermore, drug product dissolution testing can frequently detect polymorphic conversions. In rare cases, solid state characterization may have to be employed.

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## LEGEND

Figure 1(a): Decision Tree #1. Investigating the need to set acceptance criteria for polymorphs in drug substances and drug products in ANDAs for solid dosage forms or liquids containing undissolved drug substance

Figure 1(b): Decision Tree #2. Investigating how to set acceptance criteria for polymorphs in drug substances in ANDAs for solid dosage forms or liquids containing undissolved drug substance

Figure 1(c): Decision Tree #3. Investigating the need to set acceptance criteria for polymorphs in drug product in ANDAs for solid dosage forms or liquids containing undissolved drug substance

# HIV-Associated Wasting

**HIV InSite Knowledge Base Chapter**
**November 2003**

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## Introduction

The U.S. Centers for Disease Control and Prevention (CDC) recognized wasting as an AIDS-defining condition in 1987. The "wasting syndrome" is defined as a weight loss of at least 10% in the presence of diarrhea or chronic weakness and documented fever for at least 30 days that is not attributable to a concurrent condition other than HIV infection itself.(1) In practice, any involuntary weight loss of that magnitude is typically considered wasting.

A significant relationship between weight loss and mortality, disease progression, or both has been demonstrated in numerous prospective and retrospective studies both before the advent of effective antiretroviral therapy (ART) (2-11) and in the current era of treatment, in regions where such therapy is available.(12,13) In addition to weight loss, depleted levels of body cell mass, which contains the metabolically active tissue, have been associated with increased risk of mortality in patients with HIV infection.(2,5,6) It is important to note that death from malnutrition in patients with AIDS occurred at the same degree of depletion of weight and body cell mass (66% and 54% of normal, respectively) (2) as was seen in historical reports of death from starvation.(14,15) Body mass index (BMI; see www.cdc.gov/nccdphp/dnpa/bmi/index.htm), calculated by dividing an individual's weight in kilograms by the square of his or her height in meters, also has predictive value. Evaluation of data from a large French cohort studied between 1985 and 1997 found hazards ratios for death of 2.2 and 4.4 for BMIs of 16.0-18.4 and <16.0 kg/$m^2$, respectively, after adjusting for other factors that affect mortality ($p < .0001$ in each case).(11) In this same study, weight losses of <5%, 5-10%, and >10% were associated with hazards ratios for death of 1.9, 3.3, and 6.7, respectively ($p < .0001$ in each case).

The prevalence of wasting as an initial AIDS-defining diagnosis was estimated to range up to 37% in surveys performed before the advent of effective ART.(16-22) Some reports suggest that the incidence of wasting has declined since the introduction of effective ART,(22,23) but data from other studies indicate that wasting remains a significant complication, even in populations with widespread access to effective ART.(24-26) A recent report from a large cohort study suggested that although weight loss is an infrequent occurrence, a more gradual, progressive loss of lean tissue continues in many subjects.(27) Moreover, although weight gain (28-30) and increased muscle protein synthesis (31) may occur with initiation of ART, lean tissue is not consistently restored.(28)

Weight loss in HIV infection is characterized by depletion of both fat and lean tissue.(32-39) Rapid weight loss has been associated with acute infections,(40,41) whereas more gradual weight loss has been associated with malabsorptive disorders.(41) Patients with HIV

infection have also been shown to experience periods of weight stability and weight gain.(41)

## Pathophysiology

Factors that have been demonstrated or hypothesized to contribute to wasting include metabolic alterations, anorexia, malabsorptive disorders, hypogonadism, and excessive cytokine production. Because wasting in most cases results from a combination of factors or failed compensatory responses, the diagnostic process must recognize the possibility of multiple etiologies.

### Metabolic Alterations

Increased resting energy expenditure (REE) is a common finding in patients with HIV infection,(40,42-49) particularly in those with systemic secondary infections.(40,43,50) However, hypermetabolism is not a universal finding,(33,50,51) and there is no convincing causal relationship between REE and wasting. Instead, decreased energy intake has been found to be the primary contributor to wasting, particularly during periods of rapid weight loss.(40,46) Elevated REE may serve as a cofactor in accelerating weight loss and provides evidence of a failure to compensate for decreased energy intake. Studies using stable isotope techniques have demonstrated that total energy expenditure (TEE) is not significantly elevated in weight-stable patients with HIV infection, when compared with estimates of TEE in other studies of healthy adults.(46,48,52) Patients losing weight have been found to have decreased levels of TEE, despite elevated rates of REE, reflecting a decrease in physical activity levels.(46)

A variety of other metabolic alterations have also been described in HIV-infected individuals, including: increased (47,53) and decreased (54) rates of protein turnover; decreased rates of muscle protein synthesis (53); and increased rates of de novo hepatic lipogenesis,(55) lipid flux, and oxidative and nonoxidative lipid disposal.(45) As of yet, no mechanistic relationship has been demonstrated between these or other metabolic alterations and wasting. In fact, it has been shown that the reversal of wasting is not contingent upon a reversal of elevated REE.(56)

### Anorexia

As discussed above, decreased energy intake, coupled with inappropriately elevated REE, is a major factor in negative energy balance that results in weight loss. Anorexia can result from a variety of factors caused by HIV infection itself, secondary infection, and treatments for either. Painful oral and esophageal complications such as candidiasis and aphthous ulcers can reduce voluntary food intake. Nausea is a frequent adverse effect of medications. Depression, fatigue, altered taste perception, and social isolation can also contribute to anorexia or loss of interest in eating. Moreover, dosing regimens for some antiretroviral medications impose restrictions on feeding schedules that can limit the opportunities for eating.

### Hypogonadism

Impotence and low testosterone levels have been reported in men with AIDS, even in the absence of weight loss.(57-63) Decreased testosterone levels may be the result of a functional disorder of the hypothalamus,(58) primary testicular failure,(57) or both. HIV-infected men with wasting have been reported to have significantly lower total and free testosterone levels than weight-stable men.(63) In hypogonadal men with wasting, muscle mass and total body

potassium (an index of body cell mass) were found to be positively and significantly correlated with serum free testosterone levels, and exercise capacity correlated with total testosterone levels.(62) It is not yet clear whether decreased testosterone levels are a cause or consequence of wasting. A case-control study found that declines in serum bioavailable testosterone levels occurred concurrently with wasting.(64) More recently, however, data from a cohort study suggested that hypogonadism was not a factor in gradual loss of lean body mass (LBM) in men receiving effective ART.(27) In addition to malnutrition, a variety of commonly used medications, including ketoconazole, cimetidine, ganciclovir, and megestrol acetate have been associated with low testosterone levels.(60) Decreased free testosterone levels have also been found in HIV-infected women with wasting (65). The endocrine complications of HIV infection are discussed in detail in the chapter "Endocrine Manifestations of HIV."

### Gastrointestinal Disorders

Chronic diarrhea and malabsorption remain common findings in HIV-infected patients. Where ART is available, diarrhea associated with intestinal pathogens such as microsporidia, *Cryptosporidium*, *Giardia lamblia*, cytomegalovirus (CMV), and *Mycobacterium avium* has decreased, whereas ART-associated diarrhea has increased. Thus, the overall incidence rate of diarrhea has remained constant.(66) In addition to a loss of calories associated with malabsorption, diarrhea can secondarily contribute to weight loss by discouraging food intake. The quantitative contribution of diarrhea and malabsorption to wasting has not been described. The gastrointestinal complications of HIV infection are discussed in detail in the chapter "Gastrointestinal Manifestations of HIV."

### Virologic and Immunologic Factors

Cytokine disturbances have long been implicated in the metabolic disorders and wasting that accompany HIV infection.(27,67-73) For example, alterations in triglyceride (TG) metabolism, such as hypertriglyceridemia, slowed TG clearance, and increased de novo hepatic lipogenesis, correlate with elevated circulating levels of interferon alfa (IFN-alfa). (55,74) Moreover, initiation of ART in previously untreated subjects with advanced HIV infection leads to parallel reductions in IFN-alfa and TG levels.(75) Tumor necrosis factor alpha (TNF-alpha) has been variably reported to be increased or normal in patients with AIDS.(76) Increases in levels of soluble TNF receptors,(69) interleukin 1 (IL-1) receptor antagonist,(70) and IFN-alfa (71) have been observed in HIV-infected patients with weight loss. One longitudinal study linked lean tissue loss to TNF-alpha and IL-1 beta (production by circulating mononuclear white blood cells in men with HIV infection.(27) However, it cannot be determined from these studies whether the increases in cytokine levels are a cause of wasting or a concurrent manifestation of advancing HIV disease, which might accelerate lean tissue loss by some other mechanism. For example, several studies have also suggested an independent association between HIV viral load and weight loss.(77-79) Overall, the specific roles of cytokines and HIV viral load in the mechanism(s) of wasting require further study.

## Evaluation of Wasting

### Weight Loss

Although weight is measured during most routine medical assessments, its utility as a diagnostic tool has been underrecognized. The usefulness of this easily obtained measurement can be improved if serial weights are measured under standardized conditions.

(80) Ideally, weights should be recorded on the same scale; shoes, heavy clothing, and jewelry should be removed; and patients should void before weighing. Weight data obtained in this way can be used in both the diagnosis and monitoring of wasting.

Calculation of the BMI is a simple means of comparing a patient's current weight with population norms. Tables of weight for height, such as the Metropolitan Life Insurance tables,(81) can provide another means of comparing an individual's weight with population standards. The following formulas provide a simple approximation of ideal weight for height in adults: for men, 106 lbs. for the first 5 feet plus 6 lbs. for each additional inch; for women, 100 lbs. for the first 5 feet plus 5 lbs. for each additional inch.

Weight trends can be a valuable tool for monitoring a patient's nutritional status. As described earlier, rapid weight loss (>4 kg in <4 months) has been associated with episodes of acute infection (41); in fact, because weight loss may precede other clinical symptoms, it may be the first indication of infection.(40,80) In contrast, chronic or more gradual weight loss (>4 kg in >4 months) tends to reflect gastrointestinal complications.(41)

Additional factors must be considered in the evaluation of wasting in the current treatment era. For example, it is important to distinguish between voluntary and involuntary weight loss. Moreover, it is critical to be able to distinguish between classic wasting (which is more likely to occur in the context of virologic or immunologic failure, a secondary infection, or anorexia) and changes in regional fat distribution that are commonly referred to as "lipodystrophy." In addition, symptomatic hyperlactatemia has been described in patients on nucleoside analogue reverse transcriptase inhibitor (NRTI)-containing regimens and is associated with nonspecific symptoms such as rapid weight loss, abdominal pain, and fatigue,(82) and therefore might be misclassified as wasting. Metabolic complications of ART are discussed in more detail in the chapter "Metabolic Complications of HIV Therapy."

## Body Composition

Because weight loss typically consists of both fat and lean tissue, measurement of body composition for diagnostic purposes, although potentially useful, is not essential. Although several early studies demonstrated that mortality is related not just to loss of weight but also to depletion of lean tissue, a recent study performed in patients on ART suggested that weight loss was a better predictor of mortality than lean or fat tissue measured by bioelectric impedance.(13) Nonetheless, there has been considerable interest in the measurement of body composition in patients with HIV infection, and such measurements can be useful in conjunction with well-maintained weight records to characterize an individual's response to various medical or nutritional interventions.

### Bioimpedance Analysis

This technique is based on the differential resistance to a low-intensity electrical current by the fat and lean compartments of the body. Measured values of resistance and reactance obtained by bioimpedance analysis (BIA) can be used in regression equations (eg, see Kotler et al [83]) to estimate fat, LBM, and total body water. There is less consensus regarding the ability of BIA to estimate body cell mass and intracellular and extracellular water with accuracy. The equipment is relatively inexpensive and portable. A measurement takes only approximately 10 minutes and involves no pain or discomfort for the patient. However, accurate estimation of body composition using this technique depends to a large extent on accurate measurement of weight and height, as well as correct and consistent positioning of electrodes. Because there are no population standards for fat or lean tissue, BIA cannot be used to diagnose wasting. However, careful and consistent measurements with BIA can be useful for monitoring changes over time.

### Anthropometry

Sequential measurements of midarm circumference, using a tape measure, and triceps skinfold, using calipers, can be used as surrogate indicators of change in arm muscle circumference, which has been shown to predict survival in other catabolic illnesses.(84) Although these and other anthropometric measurements can also be used to estimate whole-body composition, the equations used in such calculations have not been validated in patients with HIV-associated wasting. Anthropometric measurements are highly technique dependent. Duplicate or triplicate measurements should be obtained by a trained clinician, and serial measurements should be performed by the same individual whenever possible.

### Other Techniques

There are a variety of other research methods for measuring whole body composition, including dual-energy x-ray absorptiometry (DEXA), dilution techniques, underwater weighing, magnetic resonance imaging (MRI), computed tomography (CT), total body electrical conductivity (TOBEC), and whole-body counting of potassium, nitrogen, and other elements. Regional body composition analysis can be performed using DEXA, MRI, or CT. All of the techniques listed provide more accurate estimates of body composition than BIA or anthropometry but generally involve more costly equipment and a require a greater degree of patient cooperation and time. Although useful in research, they are not considered to be necessary for standard nutritional assessment.

## Gastrointestinal Evaluation

As discussed earlier, a slow weight loss pattern has been typically associated with malabsorptive disorders, and a gastrointestinal evaluation might be indicated in such individuals if no other explanation for wasting is evident. Malabsorption can occur in the absence of diarrhea, so the presence of gastrointestinal disorders should not be excluded on the basis of normal bowel patterns alone. The evaluation of gastrointestinal symptoms associated with HIV infection are discussed in detail in the chapter "Gastrointestinal Manifestations of HIV."

## Endocrine Evaluation

Although a variety of endocrine disturbances have been documented in patients with HIV infection, hypogonadism is of primary concern in patients with wasting. In men with wasting, serum testosterone levels should be measured. Some clinicians believe that free or bioavailable testosterone levels are a more accurate diagnostic tool than total testosterone levels. In the absence of specific evidence of impairment of other hormone systems, additional endocrine evaluations for wasting are not warranted.

## Nutritional Assessment

Patients with wasting should undergo a comprehensive dietary assessment including diet history, estimation of current energy intake, and identification of factors that might interfere with food intake. Quantitative estimation of daily energy intake, along with macro- and micronutrients, should be obtained by a trained dietitian, using techniques such as diet history, 24-hour recall, or prospective food intake diaries. Food frequency questionnaires are not considered reliable for estimating an individual's energy intake. Because there is wide interindividual variability in the accuracy of self-reported food intake, this information should be considered in conjunction with an individual's weight history and current disease state.

## Interventions for Wasting

### Management of Primary and Secondary Infections

It has long been recognized that treatment of the underlying primary or secondary infection can result in weight gain in patients with HIV infection.(28,29,85,86) Obtaining meaningful prospective weight data from controlled trials of ART has been complicated by the occurrence of lipoatrophy (regional fat loss) in many patients. Although the full impact of long-term ART on wasting is not known, aggressive management of primary HIV infection remains an important component of the treatment and prevention of wasting.

Treatment of secondary infections and other complications of HIV infection is also an important factor in the management of wasting, as first evidenced by an increase in weight and body cell mass in patients with disseminated CMV infection treated with ganciclovir.(87) Opportunistic infections that interfere with swallowing (such as candidal, herpes, or CMV esophagitis) render patients particularly susceptible to wasting. In addition to secondary infections, aphthous ulcers, chronic diarrhea, or malabsorption of any etiology; depression; and other contributors to anorexia should be treated.

### Nutritional Interventions

Nutritional strategies to forestall or reverse wasting must work to maintain or increase energy intake. Patients with HIV infection can increase protein synthesis rates during periods of increased dietary intake.(47,88) However, nutritional supplementation alone is unlikely to fully restore weight or lean tissue in patients with HIV infection.

Dietary counseling by a registered dietitian can help individuals identify target energy intake and food choices to suit individual tastes, practices, and tolerances; should emphasize the importance of maintaining energy intake, even during periods when eating is not pleasurable; and can give patients techniques for managing HIV- or medication-related symptoms such as anorexia, early satiety, nausea, vomiting, diarrhea, food intolerances, and oral or esophageal ulcers. Because HIV-infected persons are at increased risk for food-borne infections, food safety is also an important component of dietary counseling. Patients who have received nutrition education can also make more informed evaluations of claims by faddists who put forth expensive and potentially harmful nutritional regimens.

At present, there are no universally accepted HIV-specific recommendations for intake of energy or macronutrients. TEE in weight-stable HIV-infected individuals is comparable to that seen in healthy subjects,(46,48,52) so the target ranges for energy intake derived from the Recommended Dietary Allowances for adults could be applied (33-44 and 29-44 kcal/kg in men and women, respectively).(89) However, individual requirements vary more widely in persons with HIV infection, owing to the variable presence of increased rates of REE or reduced activity levels. The recommended level of protein intake in healthy adults is 0.8 g/kg, and although no specific protein requirements have been determined for HIV-infected patients, it is frequently recommended that they consume 1.5 g/kg per day. However, there are currently no empiric data to support this recommendation.

Decreased serum levels of micronutrients are a frequent finding in HIV-infected patients and most likely reflect poor nutritional intake (eg, see Coodley et al [90]). Although decreased serum concentrations of selected vitamins and minerals have been associated with increased rates of disease progression and mortality in patients with HIV infection, there have been no

controlled prospective studies demonstrating that supplementation with any vitamin or mineral reverses wasting. Thus, unless a patient has evidence of specific nutrient deficiencies, a generic, low-cost daily multivitamin and mineral supplement should suffice.

### Oral Nutritional Supplementation

Increases in net daily energy intake can be achieved with the use of oral supplements, despite some compensatory decrease in self-selected food consumption. Such supplements can be very useful in individuals for whom an inability or unwillingness to prepare or consume meals becomes an impediment to oral intake. A variety of liquid and solid oral supplements are available, including conventional preparations and specialized formulas for patients with specific intolerances (eg, fat malabsorption or lactose intolerance). Elemental formulas provide another option for individuals with malabsorptive disorders. Some small studies suggest an increased benefit from special oral preparations containing specific amino acids and proprietary agents for people with HIV infection.(91-95) However, until further data become available, the primary criteria for selection of a specific supplement should be tolerability and cost.

### Nonvolitional Feeding

In the short term, repletion or maintenance of weight by enteral or parenteral routes might be considered in individuals who are unable to meet nutritional goals with oral intake because of profound anorexia, nausea, oral or esophageal lesions, diarrhea, or neurologic disorders, but in whom there is potential for stabilization or improvement. Although it may be common for patients receiving enteral or parenteral feeding to gain weight,(96-103) increases in LBM are a less consistent finding.(96,97,99,100) Two studies suggest that survival may be increased in patients receiving enteral or parenteral nutritional support, when compared with those receiving standard nutritional counseling (104) or those who decline supplemental feeding. (98) A major factor in choosing a specific nonvolitional feeding technique is the importance of using the gastrointestinal tract to the greatest extent possible.

### Enteral Feeding

Individuals with full or mildly impaired gut function might be candidates for short-term nasogastric tube feeding or, for longer periods, percutaneous endoscopic gastrostomy (PEG) or percutaneous endoscopic jejunostomy (PEJ). In some cases these approaches can use standard or elemental enteral formulas, so the cost of the nutrition itself is considerably less than for parenteral feeding. Placement of the PEG tube is a relatively simple procedure, and routine care and maintenance can be performed by the patients at home. The most common complication is superficial skin infection; other potential complications include aspiration, necrotizing fasciitis, and colocutaneous fistulas.

### Parenteral Nutrition

Provision of central or peripheral parenteral nutrition may nutritionally stabilize and maintain hydration in patients who experience a loss of gastrointestinal function. The costs and risks of this therapeutic maneuver are greater than for enteral approaches, and there is no widespread consensus regarding the appropriate use of this technique in individuals with advanced HIV infection.

## Pharmacologic Treatments

## Appetite Stimulants

### Megestrol Acetate

A synthetic progestational agent, megestrol acetate, has been shown to be a potent appetite stimulant and is approved by the U.S. Food and Drug Administration (FDA) for the treatment of HIV-associated anorexia. In two randomized, double-blind, placebo-controlled trials of patients with HIV-associated weight loss who were studied before the availability of effective ART, treatment with megestrol acetate significantly increased food intake, weight, self-reported appetite, and sense of well-being.(105,106) In one of these trials, doses of 100, 400, and 800 mg/day were compared, and energy intake, weight, and sense of well-being increased in a dose-dependent manner.(105) In both trials, the majority of weight gained was fat. For example, patients treated with 800 mg megestrol acetate per day for 12 weeks gained an average of 3.5 kg, but only 1.1 kg was LBM.(105) In another trial, treatment with the same dose of megestrol acetate resulted in a 4.5-kg increase in fat with no change in LBM over a comparable treatment period.(106 Weight gain of an even greater magnitude was reported in an open-label pharmacokinetic study of megestrol acetate, but body composition was not measured.(107) It should be noted that healthy, HIV-negative subjects who lose weight due to voluntary or involuntary restriction of energy intake also tend to regain a disproportionate amount of fat during the early stages of weight recovery.(108) However, the failure of HIV-infected patients treated with megestrol acetate to gain LBM may also derive from the hypogonadism that has been shown to occur in men treated with this agent.(60,109) To determine whether testosterone replacement could improve the proportion of weight gained as LBM in patients receiving megestrol acetate, a multicenter study was performed in which men with wasting were treated with megestrol acetate (800 mg/day) and randomly assigned to receive a replacement dose of testosterone enanthate (200 mg every other week by intramuscular injection) or placebo.(110) Most of the participants in this study received effective ART. Preliminary data suggest that, consistent with earlier studies, there was significant weight gain with megestrol acetate, but, in contrast to previous studies, approximately half of the weight gained was lean tissue. Coadministration of testosterone in replacement doses was not associated with this increase in lean tissue accrual. However, sexual functioning was retained in those who received testosterone and diminished significantly in those on placebo during megestrol acetate treatment.

In addition to hypogonadism, adrenal suppression,(110,111) deep venous thrombosis,(112) and avascular necrosis (113) have been reported in patients receiving megestrol acetate.

### Dronabinol

A synthetic form of delta-9 tetrahydrocannabinol (an active ingredient in marijuana), dronabinol is approved by the FDA for treatment of HIV-associated anorexia. Although open-label studies of dronabinol in patients with cancer (114,115) and HIV infection (116) demonstrated a consistent improvement in self-reported appetite, weight did not increase consistently. A double-blind, placebo-controlled, crossover study of dronabinol in a small number of HIV-infected men with weight loss produced no significant increases in weight or self-reported appetite or energy intake.(117) There was also no significant increase in weight in a larger, randomized, double-blind, placebo-controlled, multicenter trial of dronabinol in patients with HIV-associated weight loss.(118) Average weight change in patients randomized to receive dronabinol (2.5 mg two times per day; n = 50) was +0.1 kg over the 6-week treatment period, as compared with -0.4 kg in those who received placebo (n = 38; p = .14). Although there was no change in weight, self-reported appetite, nausea, and mood improved significantly over the treatment period. In a pharmacokinetic study, patients treated with dronabinol alone failed to gain weight, and those who received dronabinol in combination with megestrol acetate experienced no greater weight gain than those who received megestrol acetate alone.(107)

Some patients have suggested that smoked marijuana may be more effective than dronabinol because the dose can be more effectively titrated to the desired effect. Recently, the effects of smoked marijuana, oral dronabinol, and oral placebo on virologic and immunologic parameters were evaluated in a 3-week, randomized, partially blinded, metabolic ward study.(119) Subjects were allowed to eat ad libitum during the study. Significant weight gain occurred in all three groups, with greater weight gain seen in the two groups randomized to treatment with cannabinoids. However, in all three groups, the composition of the weight gained was predominantly (~80%) fat, and there was a tendency toward greater fat accrual in the central, rather than peripheral regions.(120) The most frequently reported adverse effects of dronabinol are euphoria, dizziness, and thinking abnormalities.(118)

#### Other Drugs Used to Stimulate Appetite

The antihistamine cyproheptadine increased energy intake and weight in a small open-label study in patients with HIV-associated weight loss.(121) Glucocorticoids have also been used to stimulate appetite, but these agents have specific protein catabolic effects and are therefore not recommended as a therapy for HIV-associated wasting.

### Protein Anabolic Agents

#### Recombinant Human Growth Hormone

Administered in pharmacologic doses, recombinant human growth hormone (GH) caused significant weight gain and retention of nitrogen and potassium during a short-term metabolic ward study,(45) and increases in weight and LBM in a 3-month open-label study.(122) In a randomized, double-blind, placebo-controlled trial in 178 patients with HIV-associated wasting, treatment with GH (0.1 mg/kg/day) for 3 months produced sustained and significant ($p < .001$ vs placebo) increases in weight (+1.6 kg) and LBM (+3.0 kg) that were accompanied by a decrease in fat (-1.7 kg).(123) Treadmill work output at volitional exhaustion increased significantly in patients treated with GH, and changes in work output and time to exhaustion were significantly and positively correlated with changes in LBM. Adverse effects included arthralgias, myalgia, puffiness, and diarrhea, which generally responded to dose reduction. All patients were required to be maintained on ART throughout the study, and there was no acceleration of viral replication with GH. Preliminary results from a recently completed study in 757 HIV-infected patients with 10% weight loss indicate that GH (6 mg daily or every other day) increased LBM, decreased fat, and improved performance on a cycle ergometer in patients in the current treatment era,(124) thus confirming the results of prior studies treatment.

In two separate placebo-controlled trials, combinations of pharmacologic doses of insulinlike growth factor-1 (total 10 mg/day) with smaller doses of GH (total 1.4 mg/day [125] or 0.7 mg/day[126,127]) produced increases in LBM that were comparable to or less than those obtained with GH alone.

#### Short-Term Growth Hormone for Acute Wasting

Because weight loss in patients with HIV infection occurs most rapidly during episodes of acute secondary infection, it has been hypothesized that treatment during these periods might prevent or mitigate this weight loss.(41) Two randomized, double-blind, placebo-controlled studies of short-term treatment with GH in HIV-infected subjects with newly diagnosed opportunistic infections have shown that treatment with GH can induce weight gain and accrual of LBM.(128,129) However, it is unclear whether there is any long-term advantage to such short-term treatment. Because treatment with GH in non-HIV-infected patients hospitalized in an intensive care unit has been associated with greater mortality rates,(130) GH treatment is contraindicated in HIV-infected patients during critical illness. However, it

should be noted that no such deleterious effects were observed in the two aforementioned studies of GH treatment in HIV-infected patients with mild to moderately severe secondary infections.

The FDA granted accelerated approval for GH in HIV-associated wasting at a dose of 6 mg/day for patients with weight >55 kg and lower doses for weight <55 kg. The cost of this recombinant agent limits its accessibility, and the optimal therapeutic and maintenance dosing regimens have not yet been identified. Data are limited regarding whether weight is maintained following discontinuation of GH treatment.

## Anabolic/Androgenic Steroids

Several injectable, oral, and transdermal anabolic/androgenic steroids, varying in the extent of their anabolic and androgenic properties and their potential for toxicity, are being used to treat wasting and symptoms of hypogonadism in patients with HIV infection. Testosterone is approved for treatment of hypogonadism. Nandrolone decanoate and oxymetholone have FDA approval for treatment of anemia. However, it should be emphasized that currently, apart from low doses of oxandrolone, wasting is not an approved indication for use of any of these agents.

### Testosterone

In HIV-negative hypogonadal men, testosterone replacement produced striking increases in weight and LBM.(131,132) In randomized, double-blind, placebo-controlled studies of HIV-positive men with reduced serum testosterone levels, weight and LBM have also increased after testosterone treatment, but to a more modest extent than in hypogonadal HIV-negative men.(133-136) These less robust responses may be a result of the fact that in all of the studies in men with HIV infection, the average baseline serum testosterone levels were not as low as those in the seronegative men.

Two randomized, placebo-controlled studies of injectable testosterone, alone or in combination with resistance exercise, have also been performed in HIV-infected men with wasting, one using a replacement dose (100 mg/week) in men with low serum testosterone levels (137) and the other using a supraphysiologic dose (200 mg/week) in eugonadal men. (138) In both studies, significant increases in LBM occurred with either testosterone or exercise, and in the latter study these effects tended to be additive. Taken together, these studies suggest that testosterone can increase LBM, muscle mass, and function in men with wasting and low serum testosterone levels, and a pharmacologic dose can similarly improve lean tissue in eugonadal men with wasting. In some cases, these changes have been associated with improvements in self-assessed quality of life and indices of depression.(139)

Based on evidence suggesting that HIV-infected women with wasting may have lower free testosterone levels than seronegative controls,(65) a randomized, double-blind, placebo-controlled study was performed in 53 women with HIV-associated wasting.(140) A specially prepared transdermal system was developed to deliver 0, 150, or 300 (μg/day in the three study groups. A significant increase in weight (+1.9 kg [4%]) was seen in the women receiving physiologic testosterone (150 (μg/day), but the weight gain was primarily fat.

Physiologic testosterone replacement has not been associated with significant adverse effects in any of the aforementioned studies in men. However, testosterone in pharmacologic doses decreases high-density lipoprotein (HDL) cholesterol levels, and thus might increase risk of cardiovascular disease. In addition, the effects of pharmacologic testosterone on the risk of prostate cancer in the setting of HIV infection are unknown. Testosterone enanthate or cypionate is administered by intramuscular injection. Transdermal preparations (both by

patch or gel) for men are also commercially available.

**Nandrolone Decanoate**

An injectable derivative of 19-nortestosterone, nandrolone decanoate has a relatively long half-life. Although nandrolone is approved only for the treatment of anemia associated with chronic renal failure, there has been considerable off-label use of this agent in patients with HIV infection. Significant increases in weight and LBM (generally 3-4 kg) have been seen in open-label studies in men using doses ranging from 100 mg every 2 weeks to 600 mg/week for treatment periods of 12-16 weeks.(141-144) Studies using higher doses have not produced proportionally greater increases in LBM. In one study, subjects who were randomly assigned to undergo supervised progressive resistance exercise during nandrolone treatment had greater increases in weight, LBM, and strength than those receiving nandrolone with no exercise, demonstrating that the protein anabolic effects of nandrolone can be augmented by concurrent resistance exercise.(144)

In preliminary reports from separate randomized, double-blind, placebo-controlled studies in men (145) and women (146) with a documented weight loss of >=5%, treatment with nandrolone (200 mg/week in men and 100 mg every other week in women) for 12 weeks was associated with significant increases in LBM with no changes in fat. Men who were randomized to nandrolone had significant decreases in total testosterone, sex hormone-binding globulin, follicle-stimulating hormone, luteinizing hormone, and HDL cholesterol levels, and increases in hemoglobin and hematocrit. In women, some hoarseness and hirsutism were reported. Nandrolone had no significant effect on liver enzymes in either study.

**Oxandrolone**

An oral testosterone derivative, oxandrolone is approved by the FDA as a short-term treatment for weight loss incurred in conjunction with surgery, chronic infection, trauma, or prolonged use of corticosteroids. There is no HIV-specific indication for this agent. At the approved dosing level (5-20 mg/day), there appears to be less potential for virilizing effects and hepatic toxicity than has been seen with other oral agents. In a placebo-controlled study in 63 HIV-infected men with >10% weight loss, those randomized to receive oxandrolone in a dose of 15 mg/day gained an average of 0.6 kg at the end of the 16-week study period; weight was unchanged in those who received 5 mg/day and decreased in those on placebo (-1.1 kg).(147) The composition of the weight change was not measured. Oxandrolone treatment was associated with improvements in self-reported appetite and activity, and there were no reported toxicities. In HIV-infected men with weight loss, a 20-mg/day dose of oxandrolone in combination with resistance exercise and testosterone replacement produced striking increases in LBM (+6.9 kg) and indices of strength.(148) As with pharmacologic testosterone and nandrolone, oxandrolone treatment in this latter study produced significant decreases in HDL cholesterol. Higher doses of oxandrolone have been studied in HIV-associated wasting, but no data are available on either safety or efficacy.

**Oxymetholone**

Another oral agent, oxymetholone, was reported to produce weight gain (mean 5.7 kg) and improvements in Karnofsky score in an early open-label study in patients with HIV-associated weight loss.(149) More recently, a double-blind, placebo-controlled study was performed in which 92 men and women with wasting received oxymetholone in total daily doses of 100 or 150 mg or placebo.(150) Preliminary data indicate that both dosing levels of oxymetholone produced significant increases in weight and LBM (+3.7 and +2.7 kg for weight and LBM, respectively, in the group that received 100 mg/day). However, elevations in liver enzymes occurred in 14% of patients receiving oxymetholone. Compared to the 150-

mg/day dose of oxymetholone, 100 mg/day appeared to have equivalent efficacy with less toxicity. Oxymetholone is currently approved as a treatment for anemia, but not for wasting.

### Cytokine Modulation

Because excessive generation of cytokines in response to infection has been associated with metabolic disturbances, anorexia, and wasting, several investigators have studied the effects of relatively weak suppressors of cytokine production in patients with HIV-associated wasting. Agents studied to date include three putative suppressors of TNF-alpha: thalidomide, pentoxifylline, and ketotifen, as well as dietary omega-3 fatty acids, which reduce IL-1 and TNF-alpha production by white blood cells.(151)

#### Thalidomide

The effects of thalidomide in patients with HIV-associated weight loss have been evaluated in three randomized, double-blind, placebo-controlled studies.(152-154) In the largest study of the three, 100 patients were randomized to receive thalidomide in doses of either 100 or 200 mg (nightly) or placebo for 8 weeks.(154) Patients randomized to either dosing level of thalidomide experienced modest but significant increases in weight (~4%). Treatment with a higher dose (200 mg) did not result in a better rate of weight gain and was associated with increased frequency of adverse effects and higher dropout rate. Other studies of thalidomide in patients with HIV infection have shown dramatic reversal of oral aphthous ulcers in a placebo-controlled clinical trial,(155) and reductions in stool frequency in patients with chronic diarrhea.(156) In each case, increases in weight accompanied improvement in symptoms. The most prevalent adverse effects of thalidomide in patients with HIV infection have been somnolence, peripheral neuropathy, hypersensitivity, and neutropenia.

Despite evidence that thalidomide decreases HIV replication and TNF-alpha production in vitro, plasma levels of HIV RNA and TNF-alpha were found to increase modestly (0.3-0.4 log for HIV RNA) in two recent clinical trials of this agent.(154,155) Although the durability and clinical significance of these increases are not known at this time, they have created uncertainty about the potential role for thalidomide in the treatment of wasting in patients with HIV infection.

Thalidomide is available as a treatment for erythema nodosum leprosum. Because of the well-documented and tragic teratogenic effects in infants whose mothers used this drug during pregnancy, thalidomide can be obtained only through specially licensed prescribers and pharmacists, and patients treated with this agent must adhere to strict guidelines for prevention of conception.

#### Other Cytokine Suppressors

Small studies of a variety of other weak cytokine suppressors, including pentoxifylline,(157-159) omega-3 fatty acids (fish oil [160,161], and ketotifen [either alone (162) or in combination with oxymetholone (149)]) have produced results that are modest at best and provide no compelling rationale to pursue these agents as treatments for HIV-associated wasting.

## Exercise

Exercise (both aerobic and resistance) is an excellent nonpharmacologic means of maintaining or restoring fitness level and LBM in patients with HIV infection. In an early

study, progressive resistance training was reported to increase upper and lower body strength and weight in individuals recovering from acute *Pneumocystis* pneumonia.(163) More recently, increases in weight, LBM, strength, and functional performance have been noted in HIV-positive patients undergoing progressive resistance training, alone or in combination with anabolic steroids.(137,138,148,164-166) Studies have shown that moderate exercise is safe in patients with HIV infection, with no apparent deleterious effects on immune function (167,168) or viral load.(169)

## Summary and Recommendations

Wasting continues to contribute to increased mortality and morbidity in patients with HIV infection, even in populations with access to effective ART. Thus, it remains important to monitor weight, minimize the impact of disease factors that can contribute to wasting, and intervene to mitigate or reverse weight loss when necessary. Maintenance of adequate food intake is essential in this effort, and dietary measures should be the foundation upon which other interventions are built. Patients should be encouraged to maintain or increase activity levels and to engage in moderate resistance exercise training when possible. A variety of pharmacologic measures including appetite stimulation and the use of protein anabolic therapies have been shown to be effective in promoting weight gain and lean tissue accrual. Such interventions have been demonstrated to improve functional capacity and quality of life, although further research is required to determine whether reversal of wasting improves survival.

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## HIV Nutrition & Health

## Unintentional Weight Loss/Wasting

by Jean Kressy, MS, RN, with Christine Wanke, MD, and Jül Gerrior, RD

**What is weight loss/wasting?**

Although there is more than one definition of **wasting**, nutrition experts at Tufts use the word to describe patients who unintentionally lose five percent of their body weight in a period of six months. In addition to weight loss, patients with **wasting** can experience changes in body tissue, specifically a loss of muscle (body mass) and an increase in fat. Because **wasting** can be a sign of progression of the disease, it's a red flag for clinicians. All **HIV**-positive patients, including those on anti-retroviral therapy, can develop **wasting**. A patient's appearance is not always a reliable indication of **wasting**; in patients experiencing body shape changes from fat redistribution (lipodystrophy), signs of **wasting** may be hidden. Therefore, physicians and nutritionists should routinely monitor patients for changes in body mass and weight.

**What causes weight loss/wasting?**

The link between **HIV** infection and weight loss, while not completely understood, has many causes. The most frequent explanations include side effects such as nausea or loss of appetite, medications that patients take to control their disease, opportunistic infections which increase calorie needs, mouth or tooth infections which make eating difficult, and overwhelming fatigue which makes it hard to manage everyday routines,

**Contents**

including shopping and cooking. Diarrhea, a common problem for **HIV**-positive people, may be directly related to weight loss. With or without diarrhea, malfunction of the intestine may lead to an inability to absorb nutrients (malabsorption) and may also contribute to weight loss. Changes in metabolism, including the number of calories patients expend at rest or in physical activity, also affect weight loss. Whether **HIV**-infected people lose weight because they eat less or need more calories is unclear, but medical experts agree that something about the disease affects how the body uses calories.

**Related Resources**

- Choose snacks that work for you
- Protein & fat content of selected foods
- Fiber content of selected foods
- Omega-3 fatty acids
- Dietary guidelines: a breakdown by calorie intake

**How is wasting treated?**

**Diet:**
Diet is in the first line of attack against **wasting**. Some people may be losing weight because they are not eating enough food or the right kinds of food. Nutritionists start by calculating caloric needs of their patients and then translate the numbers into food. The day's food intake, for instance, often breaks down to six small meals or three larger meals plus two snacks. For patients who need more calories or protein, supplements such as Ensure or Instant Breakfast may be included on the list. If a patient is concerned about the quality of their diet, a good multivitamin can be taken. See "Building a High Quality Diet" for more on how to eat well while meeting caloric needs. To find an **HIV**-savvy dietitian near you, use the 'Find a Nutrition Professional' feature of the American Dietetic Association's web site at http://www.eatright.org/.

**Exercise:**
Progressive resistance exercises can also help increase weight and build muscles in **HIV** patients with **wasting**. A regular weight lifting routine, at a gym or at home is ideal, but if all that can be managed is climbing stairs and carrying groceries, they work well too. A nice bonus, especially for **HIV**-infected patients who have disease-related high blood sugar, is that exercise slows the movement of glucose into the blood.

**Drugs:**
Appetite stimulants: To treat the loss of appetite (anorexia) that is a common side-effect of **HIV** medications and the infections which accompany the disease, physicians may prescribe drugs to improve appetite. Megace and Marinol, the two most commonly used, may help patients gain weight, but they're a double-edged sword; they improve appetite, but instead of building muscle, they add fat and muscle, rather than just muscle, and like all medications, have side-effects.

**Testosterone Replacement:**
To treat loss of muscle strength and body mass, **HIV**-infected men with low levels of **testosterone** may be given the hormone, either by injection, skin patch, or a gel rubbed directly onto the skin. Called hormone replacement therapy, **testosterone** can increase muscle strength and body mass without negatively affecting CD4 cell counts, especially when patients do resistance exercises while they are taking the drug. The problems with excess **testosterone**, however, are that it reduces HDL (good) cholesterol and exacerbates liver disease, which is common in **HIV**-infected patients.

**Growth Hormone:**
Growth hormone, also given by injection, may be given to **HIV** patients to reverse the loss of muscle tissue that occurs in **wasting**. The disadvantages of growth hormone are its high cost and the fact that it must generally be given every day. Like any other medication, growth hormone has multiple side effects. The most common is joint stiffness or swelling (arthralgia). Caution should be used if there is a family history of insulin resistance or diabetes as growth hormone can cause elevations in blood glucose.

**Anabolic Steroids:**
Body-building steroids, called anabolic analogues, may help patients gain weight and increase muscle mass, but because there are questions about their safety over the long run, especially their effect on the liver, health experts hesitate to use them long-term.

**Combination Treatment:**
Careful assessment of the reason for weight loss can lead to the development of a program for weight gain for most **HIV**-infected persons. Diet and/or exercise may be recommended in combination with one or more of the drugs discussed, depending on the reason for the weight loss.

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Version date: January 26, 2006
Comments to Webmaster: med-nutrition-infection@tufts.edu

## Testosterone deficiency



Deficiency of the male hormone **testosterone**, also known as hypogonadism, can cause physical symptoms that clinically may appear to be very close to depression: chronic fatigue, loss of interest in sex and food, depressed mood and a general sense of not feeling well. Lack of **testosterone** can also lead to anaemia and osteopenia (lowered bone mineral density).

**Wasting** (loss of lean body mass) and hypogonadism are also linked, although differentiating between cause and effect is not easy. For example, Berger and colleagues found no significant relationship between low **testosterone** and **wasting**, concluding that having low **testosterone** levels did not necessarily mean **wasting** occurred (Berger 1998). Although a systematic review found that **testosterone** replacement therapy was more likely to increase lean body mass compared to nothing, that does not necessarily mean all **wasting** is caused by hypogonadism, or that hypogonadism always leads to **wasting** (Kong 2002).

Clinical experience suggests that individuals do not become symptomatic until their total **testosterone** level is about 5nM, which is around half of the normal end of the lower range value. Levels of sex hormone binding globulin (SHBG) levels can become increased during a chronic infection, leading to hypogonadism despite normal **testosterone** levels.

Low **testosterone** levels have been identified as a risk factor in the breast enlargement occasionally seen as a side-effect of some antiretroviral drug regimens (Biglia 2004). For more information, see Gynaecomastia (breast enlargement) in Symptoms and illnesses: A to Z of illnesses.

**Definitions and prevalence**
Exactly what constitutes low **testosterone** levels is open to interpretation. There are two measures of **testosterone** levels: total and free. Free **testosterone** measurements are considered more accurate and reliable, but are more expensive to carry out. Consequently, many studies looking at the prevalence and treatment of hypogonadism have only included total **testosterone** levels.

Additionally, although the normal range of total **testosterone** in the blood is between 9.7 and 38.2nM, some clinicians feel that **testosterone** levels need to be interpreted on an individual by individual basis, as 'normal' levels in one individual may be very different to those in another. Before the advent of highly active antiretroviral therapy (HAART), up to 50% of men with AIDS, and 25% of men with **HIV** were observed to be hypogonadal (Dobbs 1988). Another study found that of 127 **HIV**-positive men with or without **wasting**, 17% had total **testosterone** levels below 6.73nM, well below the lower limit of normal. Interestingly, 32% were on **testosterone** replacement therapy at the time (Berger 1998). A study of 587 **HIV**-positive males between August 1997 and January 1999 found that 20% had total **testosterone** levels below 13.9nM (Kopicko 1999).

However, a 1999 study of 148 **HIV**-positive men compared with 42 **HIV**-negative men found that 31% of the **HIV**-positive men had **testosterone** levels below 9.7nM. In this study, **testosterone** levels were generally lower in all **HIV**-positive men compared to **HIV**-negative men, and were lowest in **HIV**-positive men who had lost 2.3kg or more of weight in the preceding twelve months (Arver 1999).

**Causes of hypogonadism**
Low levels of **testosterone** can occur in both men and women with **HIV** disease, although much more is know about **testosterone** deficiency as it relates to men. The majority of **testosterone** deficiency in **HIV** disease is not caused by testicular failure (also known as primary hypogonadism), but by secondary hypogonadism. This happens when there is a disruption of hormone secretion between the hypothalamus (located in the brain) and the pituitary gland (located near the brain).

Since the pituitary gland secretes hormones that stimulate the production of **testosterone** in the testes, a disruption in this hormonal cascade can cause secondary hypogonadism. Arver (1999) discovered that out of the 31% of **HIV**-positive men with low **testosterone** in their study, 19% had primary and 81% had secondary hypogonadism. Although both are associated with having low levels of **testosterone**, in secondary hypogonadism other sex hormones are also found at low levels, including luteinising hormone and follicle-stimulating hormone. In contrast, in primary hypogonadism these other sex hormones are elevated.

**HIV**-related hypogonadism can be caused by a variety of factors including opportunistic infections, **wasting**, **HIV**-associated malignancies and the effects of **HIV** itself, antiretrovirals and other medications. In general, the risk of **testosterone** deficiency increases with the length of time a person has been **HIV** positive and how ill he / she has been.

**Replacement therapy**
Men produce between 3 and 10mg of **testosterone** daily, mostly in the morning and again in the evening, while women produce around 10% of this amount. Replacement therapy aims to mimic this level of production. Treatment options include intramuscular injections **testosterone** (*Sustanon*), or use of a skin patch (*Andropatch*). Studies have shown that replacement therapy can reverse **wasting** and lipodystrophy, as well as reduce fatigue, relieve depression and restore lost libido.

*Sustanon 250* is the most common method of **testosterone** replacement in the United Kingdom. It is made up of four different **testosterone** esters, providing a total of 176mg **testosterone**, which affect how quickly or slowly the **testosterone** is absorbed after injection. It is popular amongst clinicians because it is cheaper than patches. It is administered by deep, and often painful, intramuscular injection into the buttock or thigh every two to three weeks.

*Sustanon 100* contains three shorter-lasting **testosterone** esters (equivalent to a total of 74mg **testosterone**) requiring more frequent administration. However, these two standardised dosing regimens can create several problems due to high post-injection peaks and low pre-injection trough levels.

Such high doses of **testosterone** can bring about problematic feelings of aggression (known popularly as 'roid rage'), insomnia or feeling 'wired', and an abnormally high interest in sex that can become all-consuming, and lead to the possibility of sexual risk-taking.

*Andropatch 5mg* is an oval, sticky patch applied to the back, stomach, upper arms or thighs which slowly releases 5mg **testosterone** over 24 hours. The patch is also available in a 2.5g version. This provides a replacement dose close to physiological levels, although it provides a constant flow of **testosterone** through the skin, rather than mimicking natural diurnal production. However, up to 30% of users experience skin irritation and if sites are not changed frequently, and localised skin reactions can develop. There is also the problem of patch visibility, which may be considered stigmatising.

**Testosterone** gel is also available, marketed as *AndroGel* in the United States for a number of years. The German company Schering own the European distribution rights and launched *Testogel* in the United Kingdom in 2003. The alcohol-based gel comes in 5g pouches, to be applied each morning to the belly, shoulders or inner thighs (but not genitals) and dries within minutes. Preliminary reports from a study of 30 hypogonadal **HIV**-positive males who had been receiving a stable regimen of intramuscular **testosterone** who then switched to *AndroGel* were very promising. The gel was well tolerated due to the fact that it was easy to use and **testosterone** levels were stable and physiological. Quality of life scores also improved by an average of 10% compared with the intramuscular **testosterone**.

Two further gel formulations are also currently being developed. *Andractim* is a dihydrotestosterone (DHT) gel, which may be comparable to **testosterone** gel, although no studies comparing them exist. It is available in France over-the-counter at a cost of €14 a month. Another 1% **testosterone** gel, *Testim* was launched in the United States in February 2003, but has not been licensed in Europe. An trial recently found that 30% more **testosterone** was absorbed per dose in hypogonadal **HIV**-negative men on *Testim* compared with *AndroGel* (Marbury 2003). However, the clinical significance of this is unknown.

**Testosterone, depression and fatigue**

A recent study on the use of **testosterone** replacement therapy in 22 depressed **HIV**-negative men aged 30 and over indicates that hypogonadism may cause more depression than previously thought. Researchers from Harvard Medical School found that 43% of the men who had not responded to antidepressant medications had total **testosterone** levels below 12.2nM and about a third of the men with these low or low-normal levels who received 10g of 1% **testosterone** gel daily showed dramatic improvement in mood, anxiety, and other measures of depression after eight weeks, compared with placebo (Pope 2003).

An earlier non placebo-controlled study of hypogonadal **HIV**-negative men treated with intramuscular or oral **testosterone** replacement therapy found that significant reductions in anger, irritability, sadness, tiredness and nervousness, and significant improvements in energy levels, friendliness and sense of well-being were seen in all men on therapy compared with being off therapy (Wang 1996).

Grinspoon (2000) found that men with **HIV**-related **wasting** and total **testosterone** levels below 14.8nM were more likely to be depressed than those men with higher total **testosterone**, and those who received **testosterone** replacement therapy were less depressed than those received placebo.

Fatigue has also been seen to be greatly alleviated in an open-label trial of **testosterone** for 108 **HIV**-positive men with clinical symptoms of hypogonadism and a total **testosterone** level below 17.4nM: 79% were rated as having much improved energy level by the study's end (Wagner 1998)

**Contraindications for replacement treatment**

Finding the right method and dose of **testosterone** replacement may take time. Clinical signs and symptoms should be reported to a clinician, and free and total **testosterone** levels should be measured to ensure that adequate replacement levels are being reached. Although replacement doses of intramuscular or transdermal **testosterone** are not as toxic as chronic cycles of supra-physiological doses of either **testosterone** or anabolic steroids there are still a variety of adverse effects of, and contraindications to **testosterone** replacement therapy.

Replacement doses of **testosterone** do not appear to affect **HIV** viral load or CD4 or CD8 cell counts (Bhasin 1998). However, they should be avoided in people with high red blood cell counts.

Men with prostate cancer or an enlarged prostate gland should also avoid using **testosterone** replacement therapy. Intramuscular **testosterone** and **testosterone** patches caused increases in prostate-specific antigen (PSA) levels in **HIV**-negative hypogonadal men aged over 40, so it is recommended that PSA levels are tested before and after

treatment (Guay 2000).

Since **HIV** disease and antiretroviral therapy regimens can reduce levels of high-density lipoprotein (HDL; 'good' cholesterol), the additive effect of **testosterone** on HDL levels should be monitored. A meta-analysis of hypogonadal **HIV**-negative men on intramuscular **testosterone** replacement therapy found that it is associated with a small decrease in HDL cholesterol as well as declines in low-density lipoprotein (LDL) and total cholesterol levels (Whitsel 2001).

Liver function problems are not usually seen with replacement levels of **testosterone**, although acne can be a problem.

**Women and testosterone**

Although **testosterone** is considered to be a male hormone, it also occurs naturally in women. A recent study found that 26% of **HIV**-infected women with significant weight loss had total **testosterone** levels below the normal range, even in the era of HAART (Huang 2003).

Laboratory diagnosis of **testosterone** deficiency among women is difficult, however. Total **testosterone** levels may be increased as a result of increased serum concentrations of SHBG in **HIV**-positive women, and although testing for free **testosterone** levels may be more accurate, the normal ranges for women are not standardised.

There has been little research into **testosterone** replacement in women, so treating low **testosterone** among women with **HIV** has received little attention. However, Miller (1998) found that when low-dose **testosterone** patches were used on women with **HIV**-related **wasting**, both weight and quality of life improved and the development of masculine features was not reported. Similarly, a recent placebo-controlled study has shown an increase in muscle strength in women with **HIV**-related **wasting** treated with **testosterone** patches (Dolan 2004).

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**aidsmap resources**

- Palliative care

## Palliative care news

- CROI: Capsaicin patch helps relieve neuropathy
- CROI: Fish oil and fibrate combination reduces blood fats in **HIV** patients
- CROI: Side-effects, especially neuropathy and rash, common but rarely severe in two studies of African patients on antiretroviral therapy

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L14 ANSWER 1 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:722925 CAPLUS
DOCUMENT NUMBER: 141:218967
TITLE: Methods and compositions with **trans-clomiphene** for treating **wasting** and lipodystrophy
INVENTOR(S): Podolski, Joseph S.; Wiehle, Ronald
PATENT ASSIGNEE(S): Zonagen, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 12 pp., Cont.-in-part of U.S. Ser. No. 427,768.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| US 2004171697 | A1 | 20040902 | US 2003-712546 | | 20031112 |
| WO 2003005954 | A2 | 20030123 | WO 2002-US21524 | | 20020709 |
| WO 2003005954 | A3 | 20031023 | | | |
| WO 2003005954 | B1 | 20031204 | | | |
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| US 2004097597 | A1 | 20040520 | US 2003-427768 | | 20030430 |
| PRIORITY APPLN. INFO.: | | | US 2001-304313P | P | 20010709 |
| | | | WO 2002-US21524 | A2 | 20020709 |
| | | | US 2003-427768 | A2 | 20030430 |

AB The invention discloses compns. and methods useful for treating **wasting**, especially a loss of muscle mass. The present invention also discloses compns. and methods useful for treating lipodystrophy. The compns. and methods of the present invention are particularly beneficial to HIV-infected individuals.

IT Immunostimulants
(adjuvants; methods and compns. with **trans-clomiphene** for treating **wasting** and lipodystrophy)
IT Drug delivery systems
(carriers; methods and compns. with **trans-clomiphene** for treating **wasting** and lipodystrophy)
IT AIDS (disease)
Blood serum
Body weight
Bone
CD4-positive T cell
Combination chemotherapy
Erythrocyte
Human
Human immunodeficiency virus
Kidney
Lipodystrophy
Liver
Lymphocyte
Osteoblast
Platelet (blood)
(methods and compns. with **trans-clomiphene** for

treating **wasting** and lipodystrophy)

IT Hemoglobins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(methods and compns. with **trans-clomiphene** for treating **wasting** and lipodystrophy)

IT Antiestrogens
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. with **trans-clomiphene** for treating **wasting** and lipodystrophy)

IT Muscle
(modulating mass of; methods and compns. with **trans-clomiphene** for treating **wasting** and lipodystrophy)

IT Disease, animal
(**wasting**; methods and compns. with **trans-clomiphene** for treating **wasting** and lipodystrophy)

IT 50-99-7, D-Glucose, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(blood; methods and compns. with **trans-clomiphene** for treating **wasting** and lipodystrophy)

IT 57-88-5, Cholesterol, biological studies 58-22-0, Testosterone 60-27-5, Creatinine 7440-23-5, Sodium, biological studies 9000-86-6, ALT 9001-78-9, Alkaline phosphatase 9002-62-4, Prolactin, biological studies 9002-67-9, LH 9002-68-0, FSH
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(methods and compns. with **trans-clomiphene** for treating **wasting** and lipodystrophy)

IT 50-41-9, **Clomid** 15690-55-8, cis-**Clomiphene** 15690-57-0, **trans-Clomiphene**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. with **trans-clomiphene** for treating **wasting** and lipodystrophy)

L14 ANSWER 2 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:1121828 CAPLUS
DOCUMENT NUMBER: 142:49373
TITLE: Ab initio quantum mechanical study of the binding **energies** of human estrogen receptor α with its ligands: An application of fragment molecular orbital method
AUTHOR(S): Fukuzawa, Kaori; Kitaura, Kazuo; Uebayasi, Masami; Nakata, Kotoko; Kaminuma, Tsuguchika; Nakano, Tatsuya
CORPORATE SOURCE: Biotechnology, Science Solutions, Mizuho Information and Research Institute Inc., Tokyo, 101-8443, Japan
SOURCE: Journal of Computational Chemistry (2004), Volume Date 2005, 26(1), 1-10
CODEN: JCCHDD; ISSN: 0192-8651
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have theor. examined the relative binding affinities (RBA) of typical ligands, 17β-estradiol (EST), 17α-estradiol (ESTA), genistein (GEN), raloxifene (RAL), 4-hydroxytamoxifen (OHT), tamoxifen (TAM), **clomifene** (CLO), 4-hydroxyclomifene (OHC), diethylstilbestrol (DES), bisphenol A (BISA), and bisphenol F (BISF), to the α-subtype of the human estrogen receptor ligand-binding domain (hERα LBD), by calculating their binding **energies**. The ab initio fragment MO (FMO) method, which we have recently proposed for the calcns. of macromols. such as proteins, was applied at the HF/STO-3G level. The receptor protein was primarily modeled by 50 amino acid residues surrounding the ligand. The number of atoms in these model complexes is about 850, including hydrogen atoms. For the complexes with EST, RAL, OHT, and DES, the binding **energies** were calculated again with the entire ERαLBD consisting of 241 residues or about 4000 atoms. No significant difference was found in the calculated binding **energies** between the model and the real protein complexes. This indicates that the binding between the protein and its ligands is well characterized by the model protein with the 50 residues. The calculated binding **energies** relative to EST were very

well correlated with the exptl. RBA (the correlation coefficient r = 0.837) for the ligands studied in this work. We also found that the charge transfer between ER and ligands is significant on ER-ligand binding. To our knowledge, this is the first achievement of ab initio quantum mech. calcns. of large mols. such as the entire ERαLBD protein.

IT Ab initio methods
Binding **energy**
Electron transfer
Human
Hydrogen bond
Molecular orbital methods
(ab initio quantum mech. study of binding **energies** of human estrogen receptor α with its ligands: an application of fragment MO method)

IT Molecular orbital
(fragment; ab initio quantum mech. study of binding **energies** of human estrogen receptor α with its ligands: an application of fragment MO method)

IT Protein motifs
(ligand-binding domain; ab initio quantum mech. study of binding **energies** of human estrogen receptor α with its ligands: an application of fragment MO method)

IT Free **energy**
(solvation free **energy**; ab initio quantum mech. study of binding **energies** of human estrogen receptor α with its ligands: an application of fragment MO method)

IT Estrogen receptors
RL: BSU (Biological study, unclassified); CPS (Chemical process); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process)
(α; ab initio quantum mech. study of binding **energies** of human estrogen receptor α with its ligands: an application of fragment MO method)

IT 50-28-2, 17β-Estradiol, biological studies 56-53-1, Diethylstilbestrol 57-91-0, 17α-Estradiol 80-05-7, Bisphenol A, biological studies 446-72-0, Genistein 620-92-8 911-45-5, **Clomifene** 10540-29-1, Tamoxifen 68047-06-3, 4-Hydroxytamoxifen 79838-51-0 84449-90-1, Raloxifene
RL: BSU (Biological study, unclassified); CPS (Chemical process); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process)
(ab initio quantum mech. study of binding **energies** of human estrogen receptor α with its ligands: an application of fragment MO method)

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:77736 CAPLUS
DOCUMENT NUMBER: 140:210967
TITLE: Fragment molecular orbital study of the binding **energy** of ligands to the estrogen receptor
AUTHOR(S): Fukuzawa, Kaori; Kitaura, Kazuo; Nakata, Kotoko; Kaminuma, Tsuguchika; Nakano, Tatsuya
CORPORATE SOURCE: Fuji Research Institute Corporation, Tokyo, 101-8443, Japan
SOURCE: Pure and Applied Chemistry (2003), 75(11-12), 2405-2410
CODEN: PACHAS; ISSN: 0033-4545
PUBLISHER: International Union of Pure and Applied Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We examined the published data for the binding affinity of typical ligands to the α-subtype of the human estrogen receptor with use of an approx. MO method applicable to interacting mol. clusters. An ab initio procedure for "mol. fragments" proposed recently to deal with such macromols. as proteins was applied to the MO calcns. The receptor protein was primarily modeled using 50 amino acid residues surrounding the ligand. For a few ligand-receptor complexes, the binding **energy** was also

calculated with use of 241 amino acid residues contained in the entire binding domain. No significant difference was found in the calculated binding **energy** between the complex modeled with ligand-surrounding 50 amino acids and that with residues of the entire domain. The calculated binding **energy** was correlated very well with the published relative binding affinity for typical ligands.

IT Protein motifs
(LBD of ERα; fragment MO study of binding **energy** of ligands to estrogen receptor)

IT Binding **energy**
Human
Molecular orbital
Molecular orbital
(fragment MO study of binding **energy** of ligands to estrogen receptor)

IT Molecular modeling
(of ERα LBD complexed with 17β-estradiol; fragment MO study of binding **energy** of ligands to estrogen receptor)

IT Structure-activity relationship
(receptor-binding, estrogen receptor ligand; fragment MO study of binding **energy** of ligands to estrogen receptor)

IT Estrogen receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(α; fragment MO study of binding **energy** of ligands to estrogen receptor)

IT 50-28-2, 17β-Estradiol, biological studies 56-53-1, Diethylstilbestrol 57-91-0, 17α-Estradiol 80-05-7, Bisphenol A, biological studies 446-72-0, Genistein 620-92-8, Bisphenol F 911-45-5, **Clomifene** 10540-29-1, Tamoxifen 68047-06-3, 4-Hydroxytamoxifen 79838-51-0 84449-90-1, Raloxifene
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(estrogen receptor ligand; fragment MO study of binding **energy** of ligands to estrogen receptor)

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1986:454711 CAPLUS
DOCUMENT NUMBER: 105:54711
TITLE: Analysis of **clomiphene** isomers in human plasma and detection of metabolites using reversed-phase chromatography and fluorescence detection
AUTHOR(S): Baustian, C. L.; Mikkelson, T. J.
CORPORATE SOURCE: Pharm. Chem. Dep., Univ. Kansas, Lawrence, KS, 66045, USA
SOURCE: Journal of Pharmaceutical and Biomedical Analysis (1986), 4(2), 237-46
CODEN: JPBADA; ISSN: 0731-7085
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A method is described for the quant. clin. anal. of plasma concns. of E- [15690-57-0] and Z-**clomiphene** [15690-55-8], which is used in the induction of ovulation. The isomers of **clomiphene**, in addition to metabolites, are extracted from plasma with tert-Bu Me ether (MTB). The MTB layer is dried, reconstituted and an aliquot subjected to chromatog. The drug and metabolites are separated by reversed-phase HPLC. The eluent is fed into a knitted or braided, cylindrical reaction coil made of Teflon, into which is inserted a low-**energy** mercury lamp. This results in a photoinduced stilbene-to-phenanthrene oxidation yielding highly fluorescent analytes; this provides excellent sensitivity for the quantation of the intact drug isomers and the detection of presently uncharacterized metabolites. Use of the reversed-phase chromatog. mode results in elution of the polar metabolites prior to the intact drug isomers. A combination of reversed-phase chromatog. and an in-line post-column reaction coil results in a sensitive method that is more reliable and rapid than those previously reported and is applicable to the routine anal. of clin. samples. The method has been applied to individual

isomers of **clomiphene** in plasma at concns. of 0.06-600 ng/mL.

IT Blood analysis
(climiphene isomers and metabolites determination in human, by HPLC)

IT 911-45-5D, metabolites
RL: ANT (Analyte); ANST (Analytical study)
(detection of, in blood of humans by HPLC)

IT 15690-55-8 15690-57-0
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in blood of humans by HPLC, in presence of isomer)

L14 ANSWER 5 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1104415 CAPLUS
DOCUMENT NUMBER: 144:121696
TITLE: **Clomiphene** citrate effects on testosterone/estrogen ratio in male hypogonadism
AUTHOR(S): Shabsigh, Ahmad; Kang, Young; Shabsign, Ridwan; Gonzalez, Mark; Liberson, Gary; Fisch, Harry; Goluboff, Erik
CORPORATE SOURCE: Department of Urology, NY Presbyterian Medical Center, New York, NY, USA
SOURCE: Journal of Sexual Medicine (2005), 2(5), 716-721
CODEN: JSMOAN; ISSN: 1743-6095
PUBLISHER: Blackwell Publishing, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Aim. Symptomatic late-onset hypogonadism is associated not only with a decline in serum testosterone, but also with a rise in serum estradiol. These endocrine changes neg. affect libido, sexual function, **mood**, behavior, lean body mass, and bone d. Currently, the most common treatment is exogenous testosterone therapy. This treatment can be associated with skin irritation, gynecomastia, nipple tenderness, testicular atrophy, and decline in sperm counts. In this study we investigated the efficacy of **clomiphene** citrate in the treatment of hypogonadism with the objectives of raising endogenous serum testosterone (T) and improving the testosterone/estrogen (T/E) ratio. Methods. Our cohort consisted of 36 Caucasian men with hypogonadism defined as serum testosterone level less than 300 ng/dL. Each patient was treated with a daily dose of 25 mg **clomiphene** citrate and followed prospectively. Anal. of baseline and follow-up serum levels of testosterone and estradiol levels were performed. Results. The mean age was 39 years, and the mean pretreatment testosterone and estrogen levels were 247.6 ± 39.8 ng/dL and 32.3 ± 10.9, resp. By the first follow-up visit (4-6 wk), the mean testosterone level rose to 610.0 ± 178.6 ng/dL ($P < 0.00001$). Moreover, the T/E ratio improved from 8.7 to 14.2 ($P < 0.001$). There were no side effects reported by the patients. Conclusions. Low dose **clomiphene** citrate is effective in elevating serum testosterone levels and improving the testosterone/estadiol ratio in men with hypogonadism. This therapy represents an alternative to testosterone therapy by stimulating the endogenous androgen production pathway.

IT Reproductive system, disease
(hypogonadism; low dose **clomiphene** citrate was effective in elevating serum testosterone, estradiol level and improving testosterone/estradiol ratio and may be therapeutic option for hypogonadism in Caucasian male hypogonadism patient)

IT Estrogens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(low dose **clomiphene** citrate was effective in elevating serum estradiol level and improving testosterone/estradiol ratio and may be therapeutic option for hypogonadism in Caucasian male hypogonadism patient)

IT Human
Human groups
(low dose **clomiphene** citrate was effective in elevating serum testosterone, estradiol level and improving testosterone/estradiol ratio and may be therapeutic option for hypogonadism in Caucasian male hypogonadism patient)

IT Antiestrogens
(low dose estrogen receptor antagonist **clomiphene** citrate was

effective in elevating serum testosterone and improving testosterone/estradiol ratio and may be therapeutic option for hypogonadism in Caucasian male hypogonadism patient)

IT Estrogen receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(low dose estrogen receptor antagonist **clomiphene** citrate was effective in elevating serum testosterone and improving testosterone/estradiol ratio and may be therapeutic option for hypogonadism in Caucasian male hypogonadism patient)

IT 58-22-0, Testosterone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(low dose **clomiphene** citrate was effective in elevating serum testosterone and improving testosterone/estradiol ratio and may be therapeutic option for hypogonadism in Caucasian male hypogonadism patient)

IT 50-41-9, **Clomiphene** citrate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(low dose **clomiphene** citrate was effective in elevating serum testosterone, estradiol level and improving testosterone/estradiol ratio and may be therapeutic option for hypogonadism in Caucasian male hypogonadism patient)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 6 OF 94 MEDLINE on STN
ACCESSION NUMBER: 92045043 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1941294
TITLE: **Clomiphene**-induced **mood** swings.
AUTHOR: Blenner J L
CORPORATE SOURCE: School of Nursing, San Diego State University, CA 92182-0254.
SOURCE: Journal of obstetric, gynecologic, and neonatal nursing : JOGNN / NAACOG, (1991 Jul-Aug) Vol. 20, No. 4, pp. 321-7.
Journal code: 8503123. ISSN: 0884-2175.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Nursing Journals
ENTRY MONTH: 199112
ENTRY DATE: Entered STN: 19920124
Last Updated on STN: 19980206
Entered Medline: 19911219

AB A study of couples' perceptions of infertility treatment with **clomiphene** (**clomiphene** citrate) revealed **mood** swings in 9 out of 14 women using the drug. This paper describes the **mood** swings and the responses of women and their spouses. Three phases of **mood** swing response emerged from the data: lacking awareness of the relation of the **mood** swings to the drug; gaining awareness of that relation; and managing the **mood** swings. The results of the study provide important information for nurses counseling couples who are experiencing **clomiphene**-induced **mood** swings.

L14 ANSWER 7 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:557138 CAPLUS
DOCUMENT NUMBER: 129:270591
TITLE: Differential responses of estrogen target tissues in rats including bone to **clomiphene**, enclomiphene, and zuclomiphene
AUTHOR(S): Turner, Russell T.; Evans, Glenda L.; Sluka, James P.; Adrian, M. D.; Bryant, Henry U.; Turner, Charles H.; Sato, Masahiko
CORPORATE SOURCE: Departments of Orthopedics and Biochemistry and Molecular Biology, Mayo Graduate School of Medicine, Rochester, MN, 55905, USA
SOURCE: Endocrinology (1998), 139(9), 3712-3720
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal
LANGUAGE: English

AB The substituted triphenylethylene antiestrogen **clomiphene** (CLO) prevents cancellous bone loss in ovariectomized (OVX'd) rats. However, CLO is a mixture of two stereoisomers, enclomiphene (ENC) and zuclomiphene (ZUC), which have distinctly different activities on reproductive tissues and tumor cells. The purpose of the present dose response study was to determine the effects of ENC and ZUC on nonreproductive estrogen target tissues. These studies were performed in 7-mo-old female rats with moderate cancellous osteopenia that was established by ovariectomizing rats 1 mo before initiating treatment. OVX resulted in increases in body weight, serum cholesterol, endocortical resorption, and indexes of cancellous bone turnover, as well as decreases in uterine weight, uterine epithelial cell height, bone mineral d., bone **strength**, and cancellous bone area. Estrogen treatment for 3 mo restored body weight, uterine histol., dynamic bone measurements, and osteoblast and osteoclast surfaces in OVX'd rats to the levels found in the age-matched sham-operated rats. In contrast, estrogen only partially restored cancellous bone volume and uterine weight, and it reduced serum cholesterol to subnormal values. CLO was a weak estrogen agonist on uterine measurements and a much more potent agonist on body weight, serum cholesterol, and dynamic bone measurements. CLO increased trabecular thickness in osteopenic rats and was the most effective treatment in improving cancellous bone volume and architecture. ZUC was a potent estrogen agonist on all tissues investigated and had dose-dependent effects. In contrast, ENC had dose-dependent effects on most measurements similar to CLO and decreased the uterotrophic effects of ZUC. It is concluded that ENC antagonizes the estrogenic effects of ZUC on the uterus but that the beneficial effects of CLO on nonreproductive tissues in OVX'd rats is conferred by both isomers. Furthermore, the combined actions of the two isomers on bone volume and architecture were more beneficial than either isomer given alone.

IT Animal tissue
Bone
Uterus
(differential responses of estrogen target bone and other tissues **clomiphene**, enclomiphene, and zuclomiphene)

IT Estrogens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(differential responses of estrogen target bone and other tissues **clomiphene**, enclomiphene, and zuclomiphene)

IT Osteoporosis
(postmenopausal; differential responses of estrogen target bone and other tissues **clomiphene**, enclomiphene, and zuclomiphene)

IT Osteoporosis
(therapeutic agents; differential responses of estrogen target bone and other tissues **clomiphene**, enclomiphene, and zuclomiphene)

IT 911-45-5, **Clomiphene** 15690-55-8, Zuclomiphene 15690-57-0, Enclomiphene
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(differential responses of estrogen target bone and other tissues **clomiphene**, enclomiphene, and zuclomiphene)

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 8 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:666116 CAPLUS
DOCUMENT NUMBER: 125:309206
TITLE: Multivariate analysis of capillary electrophoresis separation conditions for Z-E isomers of **clomiphene**
AUTHOR(S): Benpong, Daniel K.; Honigberg, Irwin L.
CORPORATE SOURCE: Department Pharmaceutical Chemistry, Univ. Kansas, Lawrence, KS, 66047, USA
SOURCE: Journal of Pharmaceutical and Biomedical Analysis (1996), 15(2), 233-239
CODEN: JPBADA; ISSN: 0731-7085
PUBLISHER: Elsevier

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Plackett-Burman (P-B) exptl. design was used to optimize the factors affecting separation of Z and E isomers of **clomiphene** (zuclomiphene and enclomiphene, resp.) using capillary electrophoresis. The P-B design was used to simultaneously investigate the following 5 factors: buffer ionic **strength**, buffer pH, heptakis(2,3,6-tri-O-methyl)β-cyclodextrin (TMCD) concentration, methanol concentration and injection time, each at 3 levels. In addition to these, a dummy variable was added to estimate the variability of the system. Effects on resolution and anal. time were calculated Based on the information gained from the P-B design, the following set of conditions was chosen: 100 mM phosphate buffer pH 2.3, 5 mM TMCD, 5% methanol, and 1.7 s hydrodynamic injection time. These conditions gave well-resolved peaks for zuclomiphene and enlomiphene.
IT Ionic **strength**
(multivariate anal. of capillary electrophoresis separation conditions for isomers of **clomiphene**)
IT 911-45-5D, **Clomiphene**, isomers 15690-55-8, Zuclomiphene
15690-57-0, Enclomiphene
RL: ANT (Analyte); ANST (Analytical study)
(multivariate anal. of capillary electrophoresis separation conditions for isomers of **clomiphene**)
IT 55216-11-0, Heptakis(2,3,6-tri-O-methyl)β-cyclodextrin
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(multivariate anal. of capillary electrophoresis separation conditions for isomers of **clomiphene**)

L14 ANSWER 9 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:141686 CAPLUS
DOCUMENT NUMBER: 110:141686
TITLE: Polarographic studies of drugs derived from triphenylethene. II
AUTHOR(S): Fijalek, Zbigniew; Chodkowski, Jerzy; Warowna, Malgorzata
CORPORATE SOURCE: Inst. Drug Sci., Sch. Med., Warsaw, 02097, Pol.
SOURCE: Acta Poloniae Pharmaceutica (1988), 45(3), 245-51
CODEN: APPHAX; ISSN: 0001-6837
DOCUMENT TYPE: Journal
LANGUAGE: Polish
AB The dependence of peak current intensity and potential on pH, temperature, ionic **strength**, surface tension, and EtOH content was investigated for solns. of tamoxifen (I) and **clomiphene** (II) in dilute EtOH and the optimum determination parameters were chosen for an anal. purpose. Only the 1st stage of polarog. reduction was due to diffusion-adsorption processes, while the 2nd was catalytic in its character. The polarog. determination was used for anal. of I and II in substance and tablets showing good precision and accuracy.
IT Ionic **strength**
Surface tension
(**clomiphene** and tamoxifen polarog. determination in relation to)
IT 911-45-5, **Clomiphene** 10540-29-1
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in tablets, polarog.)

L14 ANSWER 10 OF 94 MEDLINE on STN
ACCESSION NUMBER: 2001381030 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10908459
TITLE: **Clomiphene** citrate for unexplained subfertility in women.
AUTHOR: Hughes E; Collins J; Vandekerckhove P
CORPORATE SOURCE: Rm HSC-4F7, Department of Obstetrics and Gynaecology, McMaster University, 1200 Main St West, Hamilton, Ontario, Canada, L8N 3Z5.. hughese@fhs.csu.mcmaster.ca
SOURCE: Cochrane database of systematic reviews (Online), (2000) No. 3, pp. CD000057. Ref: 23
Journal code: 100909747. E-ISSN: 1469-493X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010709
Last Updated on STN: 20010709
Entered Medline: 20010705

AB BACKGROUND: The effectiveness of **clomiphene** citrate has been clearly demonstrated in the treatment of sub-fertility associated with oligo-ovulation. The multiple pregnancy rate associated with **clomiphene**, however, is elevated at approximately 10%. Additional side effects associated with **clomiphene** use also include hot flashes, **mood** swings, headaches and visual disturbances. A variety of publications have raised the question of increased ovarian cancer risks associated with **clomiphene** use. Understanding the effectiveness of **clomiphene** in this patient group is therefore, extremely important. OBJECTIVES: To determine the effectiveness of **clomiphene** citrate given to women with unexplained subfertility, in a dose range of 50-250 mg for up to 10 days. The primary outcome was clinical pregnancy. SEARCH STRATEGY: RCTs were identified using the search strategies developed for the menstrual disorders and subfertility group. See review group for more information. SELECTION CRITERIA: Randomized controlled trials were included if they were relevant to the clinical question posed and reported data in treated and untreated groups. Cohort studies were excluded. DATA COLLECTION AND ANALYSIS: Eleven potentially relevant trials were identified, of which six were included in this review. All trials were assessed for quality in terms of method of randomization, completeness of follow up, presence or absence of cross-over and co-intervention. MAIN RESULTS: **Clomiphene** appeared to be superior to no treatment or placebo. The common odds ratios for clinical pregnancy per patient and per treatment cycle were 2.37 (1.22-4.62) and 2.5 (1.35-4.62) respectively. Although there was some clinical heterogeneity between studies, the results were statistically homogeneous (p>0.1). These data suggest statistically and clinically significant improvement in pregnancy rate following **clomiphene** citrate in women with unexplained infertility. REVIEWER'S CONCLUSIONS: Although the absolute treatment effect is small, given the low cost and ease of administration, **clomiphene** citrate appears to be a sensible first choice treatment for women with unexplained infertility. However, in making this treatment choice, concerns of long-term use and ovarian cancer risk, multiple pregnancy risk and minor symptoms should be discussed. Given the extensive use of **clomiphene** in ovulatory women and recent concerns associated with long term use, a definitive trial with adequate power is warranted to establish effectiveness in women with unexplained subfertility.

L14 ANSWER 11 OF 94 MEDLINE on STN
ACCESSION NUMBER: 2000112698 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10591834
TITLE: The new selective estrogen receptor modulator MDL 103,323 increases bone mineral density and bone **strength** in adult ovariectomized rats.
AUTHOR: Ammann P; Bourrin S; Bonjour J P; Brunner F; Meyer J M; Rizzoli R
CORPORATE SOURCE: Division of Bone Diseases, WHO Collaborating Center for Osteoporosis and Bone Diseases, Department of Internal Medicine, University Hospital, Geneva, Switzerland.
SOURCE: Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA, (1999) Vol. 10, No. 5, pp. 369-76.
Journal code: 9100105. ISSN: 0937-941X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000320
Last Updated on STN: 20000320
Entered Medline: 20000307

AB Selective estrogen receptor modulators (SERMs) can prevent the bone loss induced by ovariectomy (OVX), but it is not established whether they can increase bone mass and **strength** in a curative protocol in ovariectomized osteopenic animals. We investigated the influence of a SERM of the new generation, MDL 103,323, on areal bone mineral density (BMD), as measured by dual-**energy** X-ray absorptiometry, bone **strength** and remodeling in OVX osteopenic rats. Nine weeks after OVX, 8-month-old rats were divided into six groups of 10 animals. MDL 103,323 was given by gavage at doses of 0.01, 0.1 or 0.6 mg/kg body weight, 5 days a week. The effect of MDL 103,323 was compared with that of the bisphosphonate pamidronate (APD), which was injected subcutaneously at a dose of 1.6 mmol/kg body weight for 5 days every 4 weeks. Lumbar spine (LS), femoral neck (FN), proximal tibia (PT) and midshaft tibia (MT) BMD, bone **strength**, and proximal tibia histomorphometry, serum osteocalcin, urinary total deoxypyridinoline and serum insulin-like growth factor I (IGF-I) were measured. After 16 weeks of treatment, BMD changes (means +/- SEM) were -11.4 +/- 2. 2, +4.0 +/- 2.1 and +6.4 +/- 1.0% respectively in OVX controls, in rats treated with 0.1 mg/kg MDL 103,323 ($p<0.05$) and in APD-treated rats ($p<0.02$) at the level of LS; -0.4 +/- 1.1, +6.7 +/- 1.4, +7.2 +/- 1.8% ($p<0.01$ and NS) at the level of FN; and -2.6 +/- 1.2%, +5.8 +/- 1.2, +6.9 +/- 1.4% ($p<0.03$ and 0.01) at the level of PT. MDL 103, 323-treated animals had a higher trabecular bone volume, a higher number of trabeculae and smaller intertrabecular spaces compared with OVX controls. Vertebral body ultimate **strength** was 186 +/- 13, 292 +/- 16, 249 +/- 23 N ($p<0.05$) in OVX controls, MDL 103, 323-treated rats and APD-treated rats, respectively. The administration of 0.6 mg/kg of MDL 103,323 did not further increase BMD or bone **strength**, indicating a bell-shaped dose-response curve. MDL 103,323 lowered plasma osteocalcin concentration and urinary deoxypyridinoline excretion. In rats treated with 0.1 mg/kg MDL 103, 323, plasma IGF-I was increased as compared with OVX controls (664 +/- 36 ng/ml vs 527 +/- 39 ng/ml, $p<0.05$). In conclusion, these results indicate that this new SERM positively influences BMD and lumbar spine bone **strength** in estrogen-deficient rats.

L14 ANSWER 12 OF 94 EMBASE 

ACCESSION NUMBER: 1998281295 EMBASE

TITLE: Disturbance of the reproductive axis induced by negative **energy** balance.

AUTHOR: Judd S.J.

CORPORATE SOURCE: S.J. Judd, Department of Medicine, Flinders Medical Centre, Bedford Park, SA 5042, Australia. stephen.judd@flinders.edu.au

SOURCE: Reproduction, Fertility and Development, (1998) Vol. 10, No. 1, pp. 65-72. .
Refs: 67
ISSN: 1031-3613 CODEN: RFDEEH

COUNTRY: Australia
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 003 Endocrinology
010 Obstetrics and Gynecology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19980910
Last Updated on STN: 19980910

AB Animal reproduction is impaired when intake of **energy** is so restricted that activities essential to life are threatened; this is seen as a homeostatic adjustment that restricts wasteful **energy** expenditure. Fasting or exercising to a degree requiring considerable **energy** expenditure has major effects on the hypothalamus, including activation of corticotrophin-releasing factor (CRF) neurons, suppression of thyrotrophin-releasing hormone synthesis, and increased growth hormone secretion; these are associated with increased concentrations of hypothalamic neuropeptide Y mRNA and are corrected by administration of leptin, an adipose-tissue protein with a tertiary structure similar to the cytokine interleukin-2. This response to fasting results from a disordered pattern of activity in the gonadotrophin-releasing hormone (GnRH) pacemaker, characterized by reduced luteinizing

hormone pulsatility, particularly during daytime. Animal studies have suggested that the response depends on an intact afferent vagal system from the stomach and the presence of oestrogen. Noradrenergic neurons forming the A2 group increase the activity of CRF neurons that, in turn, inhibit GnRH pulsatility. Reproductive impairment due to fasting is reversed by leptin, and abnormalities of leptin are described in individuals who fast or who develop exercise-induced amenorrhoea. This paper discusses these changes induced by negative **energy** balance and speculates on the involvement of leptin as a contributor to these abnormalities.

L14 ANSWER 13 OF 94 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2003455773 EMBASE
TITLE: Use of **clomiphene** citrate in women.
SOURCE: Fertility and Sterility, (2003) Vol. 80, No. 5, pp. 1302-1308. .
Refs: 71
ISSN: 0015-0282 CODEN: FESTAS
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 010 Obstetrics and Gynecology
030 Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20031201
Last Updated on STN: 20031201

AB CC is the best initial treatment for the majority of women whose infertility is associated with ovulatory dysfunction (anovulation, luteal phase deficiency). Combined with appropriately timed IUI, CC treatment also increases cycle fecundity in couples with unexplained infertility. CC treatment generally should be limited to the minimum effective dose and to no more than six ovulatory cycles. Failure to conceive after successful CC-induced ovulation is indication for further evaluation to exclude other contributing causes of infertility. Combination therapies involving CC and other agents (met-formin, glucocorticoids, exogenous gonadotropins) may be effective when treatment with CC alone fails to induce ovulation. Alternative strategies for the CC-resistant woman include treatment with aromatase inhibitors or exogenous go nadotropins and, in selected patients, ovarian drilling. CC treatment should be monitored (BBT, serum progesterone concentration, urinary LH excretion) to ensure its effectiveness in ovulation induction. Side effects of CC treatment are generally mild and well tolerated. The principal risk of CC treatment is an increased incidence of multifetal gestation (<10%).

L14 ANSWER 14 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1995:131466 BIOSIS
DOCUMENT NUMBER: PREV199598145766
TITLE: Endocrinological change in late luteal phase dysphoric disorder treated with **clomiphene** citrate during climacterium.
AUTHOR(S): Ushiroyama, Takahisa [Reprint author]; Ikeda, Atsushi; Ueki, Minoru
CORPORATE SOURCE: Dep. Obstet. Gynecol., Osaka Med. Coll., 2-7 Daigaku-cho, Takatsuki 569, Osaka, Japan
SOURCE: Research Communications in Psychology Psychiatry and Behavior, (1994) Vol. 19, No. 1-2, pp. 1-12.
CODEN: RCPBDC. ISSN: 0362-2428.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Mar 1995
Last Updated on STN: 23 May 1995

AB We report nine climacteric women who experienced psychological symptoms, i.e., **mood** swing, with somatic symptoms such as fatigue, hot flashes, lack of **energy**, shoulder stiffness, and headache during

the late luteal phase for several months. These patients were diagnosed with late luteal phase dysphoric disorder by DSM-III-R criteria. They showed unusual endocrinological features especially in the luteal phase parallel to the development of symptoms. Four women were successfully treated with **clomiphene** citrate and their hormonal levels changed significantly during treatment.

IT Major Concepts
Behavior; Biosynchronization; Clinical Chemistry (Allied Medical Sciences); Endocrine System (Chemical Coordination and Homeostasis); Metabolism; Nervous System (Neural Coordination); Pharmacology; Psychiatry (Human Medicine, Medical Sciences); Reproductive System (Reproduction)

IT Chemicals & Biochemicals
**CLOMIPHENE** CITRATE; LUTEINIZING HORMONE; PROGESTERONE

IT Miscellaneous Descriptors
ANTIDEPRESSANT-DRUG; BEHAVIOR; **CLOMIPHENE** CITRATE; DEPRESSION; FATIGUE; FSH ESTRADIOL; HEADACHE; LUTEINIZING HORMONE; METABOLIC-DRUG; **MOOD** SWINGS; PHARMACODYNAMICS; PROGESTERONE; PSYCHIATRY; PSYCHOLOGY; SHOULDER STIFFNESS

ORGN Classifier
Hominidae 86215

Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia

Organism Name
human

Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 50-41-9 (**CLOMIPHENE** CITRATE)
9002-67-9 (LUTEINIZING HORMONE)
57-83-0 (PROGESTERONE)

L14 ANSWER 15 OF 94 MEDLINE on STN
ACCESSION NUMBER: 2005392129 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16050534
TITLE: Psychological side-effects of **clomiphene** citrate and human menopausal gonadotrophin.
AUTHOR: Choi So-Hyun; Shapiro Heather; Robinson Gail E; Irvine Jane; Neuman Jan; Rosen Barry; Murphy Joan; Stewart Donna
CORPORATE SOURCE: Women's Health Program, University Health Network, University of Toronto, Ontario, Canada.. cshi@unitel.co.kr
SOURCE: Journal of psychosomatic obstetrics and gynaecology, (2005 Jun) Vol. 26, No. 2, pp. 93-100.
Journal code: 8308648. ISSN: 0167-482X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200511
ENTRY DATE: Entered STN: 20050731
Last Updated on STN: 20051111
Entered Medline: 20051110

AB OBJECTIVE: This study evaluated the psychological side-effects of **clomiphene** citrate (CC) and hMG in women undergoing fertility treatment. METHOD: This study was a cross-sectional, self-report survey of 454 women at various stages of treatment for infertility. At the time of study, 139 women had not taken fertility drugs and 315 women had taken one or more cycles of CC or hMG. All subjects were asked to complete the State-Trait Anxiety Inventory (STAI). Women taking CC or hMG were also asked to complete a self-administered questionnaire on the side-effects of their medications. RESULT(S): In the CC group (n = 162) and hMG group (n = 153), 77.8% (126 of 162) and 94.8% (145 of 153) reported at least one side-effect, respectively. Irritability, **mood** swings, **feeling** down, and bloating had high frequencies in both CC and hMG groups, with a higher mean number of side effects reported in the hMG group (4.4 +/- 3.7 for the CC group and 6.8 +/- 3.7 for the hMG group, $p < 0.001$). There was no significant difference among the CC, hMG and no medication groups for mean state and trait anxiety scores. However, there were significant differences among the three side-effect groups (those who reported 1 to 4, 5 to 7, and more than 7 side-effects) for the mean scores

of state (df = 2, F = 8.7, p < 0.001) and trait (df = 2, F = 11.9, p < 0.001) anxiety in women taking fertility drugs. CONCLUSION(S): Women taking CC or hMG reported high frequencies of psychological side-effects, and should be advised of these before treatment.

L14 ANSWER 16 OF 94 MEDLINE on STN
ACCESSION NUMBER: 2004584938 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15521089
TITLE: Ab initio quantum mechanical study of the binding **energies** of human estrogen receptor alpha with its ligands: an application of fragment molecular orbital method.
AUTHOR: Fukuzawa Kaori; Kitaura Kazuo; Uebayasi Masami; Nakata Kotoko; Kaminuma Tsuguchika; Nakano Tatsuya
CORPORATE SOURCE: Biotechnology, Science Solutions, Mizuho Information & Research Institute, Inc., 2-3 Kanda Nishiki-cho, Chiyoda-ku, Tokyo 101-8443, Japan.. Kaori.fukuzawa@gene.mizuho-ir.co.jp
SOURCE: Journal of computational chemistry, (2005 Jan 15) Vol. 26, No. 1, pp. 1-10. Journal code: 9878362. ISSN: 0192-8651.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 20041124
Last Updated on STN: 20050114
Entered Medline: 20050113
AB We have theoretically examined the relative binding affinities (RBA) of typical ligands, 17beta-estradiol (EST), 17alpha-estradiol (ESTA), genistein (GEN), raloxifene (RAL), 4-hydroxytamoxifen (OHT), tamoxifen (TAM), **clomifene** (CLO), 4-hydroxyclomifene (OHC), diethylstilbestrol (DES), bisphenol A (BISA), and bisphenol F (BISF), to the alpha-subtype of the human estrogen receptor ligand-binding domain (hERalpha LBD), by calculating their binding **energies**. The ab initio fragment molecular orbital (FMO) method, which we have recently proposed for the calculations of macromolecules such as proteins, was applied at the HF/STO-3G level. The receptor protein was primarily modeled by 50 amino acid residues surrounding the ligand. The number of atoms in these model complexes is about 850, including hydrogen atoms. For the complexes with EST, RAL, OHT, and DES, the binding **energies** were calculated again with the entire ERalphaLBD consisting of 241 residues or about 4000 atoms. No significant difference was found in the calculated binding **energies** between the model and the real protein complexes. This indicates that the binding between the protein and its ligands is well characterized by the model protein with the 50 residues. The calculated binding **energies** relative to EST were very well correlated with the experimental RBA (the correlation coefficient r=0.837) for the ligands studied in this work. We also found that the charge transfer between ER and ligands is significant on ER-ligand binding. To our knowledge, this is the first achievement of ab initio quantum mechanical calculations of large molecules such as the entire ERalphaLBD protein.

L14 ANSWER 17 OF 94 MEDLINE on STN
ACCESSION NUMBER: 2004582181 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15559352
TITLE: Fertility after ovarian drilling by transvaginal fertiloscopy for treatment of polycystic ovary syndrome.
AUTHOR: Fernandez Herve; Watrelot Antoine; Alby Jean-Dominique; Kadoch Jacques; Gervaise Amelie; deTayrac Renaud; Frydman Rene
CORPORATE SOURCE: Service de Gynecologie-Obstetrique, Hopital Antoine Beclere, Assistance Publique-Hopitaux de Paris, Clamart, France.
SOURCE: The Journal of the American Association of Gynecologic Laparoscopists, (2004 Aug) Vol. 11, No. 3, pp. 374-8. Journal code: 9417443. ISSN: 1074-3804.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200412
ENTRY DATE: Entered STN: 20041124
Last Updated on STN: 20041222
Entered Medline: 20041221

AB STUDY OBJECTIVE: To evaluate fertiloscopy ovarian drilling with bipolar **energy** in women with **clomiphene** citrate-resistant polycystic ovary syndrome (PCOS). DESIGN: Prospective study (Canadian Task Force classification II). SETTING: University teaching hospital and private clinic. PATIENTS: Eighty women with **clomiphene** citrate-resistant PCOS. INTERVENTION: Operative transvaginal fertiloscopy with a coaxial bipolar electrode. MEASUREMENTS AND MAIN RESULTS: During a mean follow-up of 18.1 months (+/- 6.4), 73 women (91%) recovered regular and ovulatory cycles. The cumulative pregnancy rate was 60% (44/73) for spontaneous and stimulated cycles, with 39.7% (29/73) imputed to drilling alone. The mean time to conceive was 3.9 months (range 1-11.8). There were eight miscarriages (18%), and no ectopic pregnancies or multiple pregnancy. No complications occurred. CONCLUSION: Ovarian drilling by transvaginal fertiloscopy with bipolar electrosurgery appears to be an effective minimally invasive procedure in patients with PCOS resistant to **clomiphene** citrate.

L14 ANSWER 18 OF 94 MEDLINE on STN
ACCESSION NUMBER: 2002068149 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11792585
TITLE: Recovery of proximal tibia bone mineral density and **strength**, but not cancellous bone architecture, after long-term bisphosphonate or selective estrogen receptor modulator therapy in aged rats.
AUTHOR: Bourrin S; Ammann P; Bonjour J P; Rizzoli R
CORPORATE SOURCE: Division of Bone Diseases, WHO Collaborating Center for Osteoporosis and Bone Diseases, Department of Internal Medicine, University Hospital, Geneva, Switzerland.
SOURCE: Bone, (2002 Jan) Vol. 30, No. 1, pp. 195-200.
Journal code: 8504048. ISSN: 8756-3282.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020125
Last Updated on STN: 20020430
Entered Medline: 20020429

AB Various bisphosphonates and the selective estrogen receptor modulator (SERM) raloxifene are approved treatments of postmenopausal osteoporosis. They increase bone mineral density (BMD), decrease bone turnover, and reduce vertebral fracture incidence through different cellular mechanisms. We investigated the bone cellular activities, architecture, mineral content/density, and **strength** of ovariectomized (ovx) rats on a long-term bisphosphonate or SERM treatment, at doses of either agent correcting bone **strength**. Eleven weeks postovariectomy, 6-month-old rats were treated with the SERM MDL 103,323 or with the bisphosphonate pamidronate for 5 months. Doses of pamidronate and MDL 103,323 were selected from previous studies showing correction of the ovx-induced decrease of ultimate **strength** of proximal tibia. Ultimate and yield **strengths**, BMD, and histomorphometric parameters were all quantified at the same site, i.e., the proximal tibia metaphysis. Long-term pamidronate decreases bone turnover and bone formation activity, leading to trabecular thinning. MDL 103,323 decreases bone turnover to a lesser extent, and slightly protects trabecular architecture by uncoupling bone resorption and formation activities. The yield **strength** is corrected by pamidronate, but not by MDL 103,323 treatment. However, neither compound restores the ovariectomy-induced cancellous bone loss. Total tissue area and cortical thickness are unchanged with pamidronate or MDL 103,323 treatment, indicating that cortical bone mass, thickness, and cross-sectional area

are not modified. The discrepancy between proximal tibia BMD and mechanical resistance to fracture modifications, on the one hand, and cancellous bone volume, on the other hand, could be due to changes in the degree of mineralization of bone matrix and/or of the intrinsic properties of the bone matrix.

L14 ANSWER 19 OF 94 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1989:77496 BIOSIS
DOCUMENT NUMBER: PREV198987041894; BA87:41894
TITLE: EFFECT OF FEEDING **CLOMIPHENE** CITRATE ON THE PERFORMANCE OF BROILERS.
AUTHOR(S): ALI M A [Reprint author]; SHINGARI B K
CORPORATE SOURCE: DEP POULT SCI, BANGLADESH AGRIC UNIV, MYMENSINGH, BANGLADESH
SOURCE: Indian Journal of Animal Sciences, (1988) Vol. 58, No. 11, pp. 1333-1338.
CODEN: IJLAA4. ISSN: 0367-8318.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 23 Jan 1989
Last Updated on STN: 23 Jan 1989
AB Feeding **clomiphene** citrate to commercial broiler chicks depressed the growth rate, nitrogen efficiency and feed consumption, but improved the efficiency of feed and **energy** utilization at all the ages and seasons. However, the depression of growth rate and feed consumption were not dose related. The chemical had no effect on livability. The efficiency of nitrogen and **energy** utilization were better at the early age and in summer and rainy seasons than in winter and spring.
IT Major Concepts
Animal Husbandry (Agriculture); Development; Nutrition
IT Miscellaneous Descriptors
FEED EFFICIENCY GROWTH FEED INDUSTRY LIVESTOCK INDUSTRY
ORGN Classifier
Galliformes 85536
Super Taxa
Aves; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Birds, Chordates, Nonhuman Vertebrates, Vertebrates
RN 50-41-9 (**CLOMIPHENE** CITRATE)

L14 ANSWER 20 OF 94 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2005521110 EMBASE
TITLE: A pharmacotherapeutic review of treatment options for infertility in women.
AUTHOR: Moultry A.M.; Eaton A.; Che S.
CORPORATE SOURCE: Dr. A.M. Moultry, Department of Pharmacy Practice, College of Pharmacy and Health Sciences, Texas Southern University, Houston, TX, United States
SOURCE: Formulary, (2005) Vol. 40, No. 10, pp. 329-341. .
Refs: 54
ISSN: 1082-801X CODEN: FORMF
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 010 Obstetrics and Gynecology
030 Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20051215
Last Updated on STN: 20051215
AB The growing trend for women to wait later in life before having their first child has placed many women at a higher risk for difficult conception. There are numerous classes of medications available to assist

women who have been diagnosed with infertility. Agents that are used in the treatment of infertility include: **clomiphene** citrate, aromatase Inhibitors, gonadotrapins, chorionic gonadotrapins, gonadotropin-releasing hormone, gonadotropin-releasing hormone agonists, gonadotropin-releasing hormone antagonists, follitropins, and other miscellaneous agents. Medications chosen for a patient will vary depending on the identified cause of the infertility. Additionally, economic factors will play a role. It is important for healthcare professionals to be aware of treatment options and have a basic understanding of the role these medications play in the treatment of infertility.

L14 ANSWER 21 OF 94 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2005201551 EMBASE
TITLE: Neuroendocrine effects on **mood**.
AUTHOR: Spinelli M.G.
CORPORATE SOURCE: Prof. M.G. Spinelli, Department of Clinical Psychiatry, Coll. Phys. Surgs. of Columbia Univ., New York State Psychiatric Institute, 1051 Riverside Drive, New York, NY 10032, United States. mgs8@columbia.edu
SOURCE: Reviews in Endocrine and Metabolic Disorders, (2005) Vol. 6, No. 2, pp. 109-115. .
Refs: 41
ISSN: 1389-9155 CODEN: REMDCG
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
010 Obstetrics and Gynecology
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
ENTRY DATE: Entered STN: 20050616
Last Updated on STN: 20050616
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L14 ANSWER 22 OF 94 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2004387896 EMBASE
TITLE: Use of **clomiphene** citrate in women.
SOURCE: Fertility and Sterility, (2004) Vol. 82, No. SUPPL. 1, pp. S90-S96. .
Refs: 71
ISSN: 0015-0282 CODEN: FESTAS
PUBLISHER IDENT.: S 0015-0282(04)00887-8
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 010 Obstetrics and Gynecology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20040930
Last Updated on STN: 20040930

AB • CC is the best initial treatment for the majority of women whose infertility is associated with ovulatory dysfunction (anovulation, luteal phase deficiency). Combined with appropriately timed IUI, CC treatment also increases cycle fecundity in couples with unexplained infertility. • CC treatment generally should be limited to the minimum effective dose and to no more than six ovulatory cycles. Failure to conceive after successful CC-induced ovulation is indication for further evaluation to exclude other contributing causes of infertility. • Combination therapies involving CC and other agents (metformin, glucocorticoids, exogenous gonadotropins) may be effective when treatment with CC alone fails to induce ovulation. Alternative strategies for the CC-resistant woman include treatment with aromatase inhibitors or exogenous gonadotropins and, in selected patients, ovarian drilling. • CC

treatment should be monitored (BBT, serum P concentration, urinary LH excretion) to ensure its effectiveness in ovulation induction. • Side effects of CC treatment are generally mild and well tolerated. The principal risk of CC treatment is an increased incidence of multifetal gestation (<10%).

L14 ANSWER 23 OF 94 MEDLINE on STN
ACCESSION NUMBER: 2003339236 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12871884
TITLE: A prospective dose-finding study of the amount of thermal **energy** required for laparoscopic ovarian diathermy.
AUTHOR: Amer S A K; Li T C; Cooke I D
CORPORATE SOURCE: Department of Obstetrics and Gynaecology, The University of Sheffield, Jessop Wing, Sheffield Teaching Hospitals, Tree Root Walk, Sheffield S10 2SF, UK.. s.amer@sheffield.ac.uk
SOURCE: Human reproduction (Oxford, England), (2003 Aug) Vol. 18, No. 8, pp. 1693-8.
Journal code: 8701199. ISSN: 0268-1161.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 20030722
Last Updated on STN: 20040416
Entered Medline: 20040415
AB BACKGROUND: This prospective dose-finding study was undertaken to determine the optimal amount of thermal **energy** required for laparoscopic ovarian diathermy (LOD) in women with polycystic ovary syndrome (PCOS). METHODS: Thirty women with **clomiphene** -resistant PCOS were included in the study. All women underwent LOD. A modified Monte Carlo up-and-down design was utilized. Women were treated in groups of three (10 groups). The amount of **energy** applied was standardized at 150 J/puncture. The number of punctures in each group was decreased/increased according to the number of responders in the previous group. The main outcome was ovulation as defined by a serum progesterone concentration of > or =30 nmol/l. RESULTS: Four groups (n=12) were treated with four punctures/ovary, three groups (n=9) with three punctures, two groups (n=6) with two punctures and one group (n=3) with one puncture. Ovulation occurred in 67, 44, 33 and 33% of women treated with four, three, two and one puncture/ovary respectively. The corresponding pregnancy rates were 67, 56, 17 and 0%. The reductions in the free androgen index and the serum concentrations of testosterone and androstenedione after LOD were observed only in women treated with three and four punctures/ovary. CONCLUSION: The clinical response to LOD seems to be dose-dependent, with an increase in the frequency of ovulation and conception with an increasing dose of thermal **energy** up to 600 J/ovary.

L14 ANSWER 24 OF 94 MEDLINE on STN
ACCESSION NUMBER: 2001037922 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11020510
TITLE: Psychological well-being and coping patterns in infertile men.
AUTHOR: Dhillon R; Cumming C E; Cumming D C
CORPORATE SOURCE: Department of Obstetrics and Gynaecology, University of Alberta, Edmonton, Alberta, Canada.
SOURCE: Fertility and sterility, (2000 Oct) Vol. 74, No. 4, pp. 702-6.
Journal code: 0372772. ISSN: 0015-0282.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001129
AB OBJECTIVE: To determine whether differences existed in **mood** and

coping styles among fertile men, oligoasthenospermic men, or euspermic men whose wives were undergoing ovulation stimulation with **clomiphene** and IUI. DESIGN: A cross-sectional research design. SETTING: Hospital-based academic fertility clinic. PATIENT(S): 30 fertile men with currently pregnant wives, 30 euspermic and 30 oligoasthenospermic men in couples undergoing ovulation stimulation with **clomiphene** and IUI. INTERVENTION(S): Measures of psychological well-being and coping were administered. MAIN OUTCOME MEASURE(S): Biodemographic information, and psychometric measures of **mood** and coping. RESULT(S): There were no significant differences among the groups on any of the measures except the Family Inventory of Life Events (FILE), in which fertile men reported higher stress levels. FILE scores in all groups were moderate, indicating typical levels of family stress. CONCLUSION(S): **Mood** and coping in the three groups were similar. This study suggests that men's psychological adjustment to their own infertility and to unexplained infertility is generally healthy.

L14 ANSWER 25 OF 94 EMBASE 

ACCESSION NUMBER: 2003183861 EMBASE
TITLE: Measures of aggression and **mood** changes in male weightlifters with and without androgenic anabolic steroid use.
AUTHOR: Perry P.J.; Kutscher E.C.; Lund B.C.; Yates W.R.; Holman T.L.; Demers L.
CORPORATE SOURCE: Dr. P.J. Perry, S-415 Pharmacy Bldg., University of Iowa, Iowa City, IA 52246, United States
SOURCE: Journal of Forensic Sciences, (2003) Vol. 48, No. 3, pp. 646-651. .
Refs: 27
ISSN: 0022-1198 CODEN: JFSCAS
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 032 Psychiatry
037 Drug Literature Index
049 Forensic Science Abstracts
052 Toxicology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20030522
Last Updated on STN: 20030522

AB Supraphysiologic doses of testosterone are associated with increased aggression that is hypothesized to be a function of testosterone serum concentrations, **mood**, and personality. The study attempted to characterize this relationship among weightlifters who were users (n = 10) and nonusers (n = 18) of anabolic steroids. Participants were interviewed using the Modified Mania Rating Scale and Hamilton Rating Scale for Depression to assess **mood**, the Buss-Durkee Hostility Inventory (BDHI) and Point Subtraction Aggression Paradigm (PSAP) to assess aggression, and the Personality Disorder Questionnaire (PDQ-R) to assess personality. Blood samples were obtained for the determination of total, free, and weakly bound testosterone. Comparisons of continuous variables between testosterone users and non-users were performed with a parametric (unpaired t-test) or non-parametric (Mann-Whitney) test where appropriate. Correlations with testosterone were examined separately for testosterone users and non-users, using Spearman rank correlation. The subjective (BDHI) and objective (PSAP) assessments of aggression found that supranormal testosterone concentrations were associated with increased aggression. However, the PDQ-R results suggest that this finding was confounded by the personality disorder profile of the steroid users, because steroid users demonstrated Cluster B personality disorder traits for antisocial, borderline, and histrionic personality disorder.

L14 ANSWER 26 OF 94 EMBASE 

ACCESSION NUMBER: 2001260190 EMBASE
TITLE: The effects of intense exercise on the female reproductive system.
AUTHOR: Warren M.P.; Perlroth N.E.

CORPORATE SOURCE: M.P. Warren, Department of Obstetrics/Gynecology, Columbia University, 622 West 168th Street, New York, NY 10032, United States
SOURCE: Journal of Endocrinology, (2001) Vol. 170, No. 1, pp. 3-11.
.
Refs: 92
ISSN: 0022-0795 CODEN: JOENAK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
003 Endocrinology
010 Obstetrics and Gynecology
030 Pharmacology
033 Orthopedic Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20010815
Last Updated on STN: 20010815

AB Women have become increasingly physically active in recent decades. While exercise provides substantial health benefits, intensive exercise is also associated with a unique set of risks for the female athlete. Hypothalamic dysfunction associated with strenuous exercise, and the resulting disturbance of GnRH pulsatility, can result in delayed menarche and disruption of menstrual cyclicity. Specific mechanisms triggering reproductive dysfunction may vary across athletic disciplines. An **energy** drain incurred by women whose **energy** expenditure exceeds dietary **energy** intake appears to be the primary factor effecting GnRH suppression in athletes engaged in sports emphasizing leanness; nutritional restriction may be an important causal factor in the hypoestrogenism observed in these athletes. A distinct hormonal profile characterized by hyperandrogenism rather than hypoestrogenism is associated with athletes engaged in sports emphasizing **strength** over leanness. Complications associated with suppression of GnRH include infertility and compromised bone density. Failure to attain peak bone mass and bone loss predispose hypoestrogenic athletes to osteopenia and osteoporosis. Metabolic aberrations associated with nutritional insult may be the primary factors effecting low bone density in hypoestrogenic athletes, thus diagnosis should include careful screening for abnormal eating behavior. Increasing caloric intake to offset high **energy** demand may be sufficient to reverse menstrual dysfunction and stimulate bone accretion. Treatment with exogenous estrogen may help to curb further bone loss in the hypoestrogenic amenorrheic athlete, but may not be sufficient to stimulate bone growth. Treatment aimed at correcting metabolic abnormalities may in fact prove more effective than that aimed at correcting estrogen deficiencies.

L14 ANSWER 27 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:563876 CAPLUS
DOCUMENT NUMBER: 107:163876
TITLE: Polarographic studies of drugs of triphenylethene derivatives. Part I
AUTHOR(S): Fijalek, Zbigniew; Chodkowski, Jerzy; Warowna, Malgorzata
CORPORATE SOURCE: Dep. Inorg. Anal. Chem., Sch. Med., Warsaw, Pol.
SOURCE: Journal of Electroanalytical Chemistry and Interfacial Electrochemistry (1987), 226(1-2), 129-36
CODEN: JEIEBC; ISSN: 0022-0728
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Both d.c. polarog. and cyclic voltammetry were used to study tamoxifen (TX), **clomiphene** (CM) and chlorotrianisene (ChT). The dependences of the limiting currents and half-wave potentials on the pH of solution, temperature, Hg head, ionic **strength** and surface tension of the solution were studied. The optimal measuring parameters and background solns. were established. The 1st reduction wave was found to be of a diffusive-adsorptive character, and the 2nd one a catalytic wave. The reduction processes consume 2 electrons and proceed with the addition of 2 protons. Since the probability of oxidizing the reduced C:C bond is very

small, the anodic processes observed on the cyclic curves are probably caused by the anodic oxidation of TX, CM and ChT to the corresponding phenanthrene derivs. Methods of determining TX and CM in pure form and in tablets were established. Statistical anal. of the results obtained showed that these methods are characterized by good accuracy.

IT Reduction, electrochemical
(of chlorotrianisene and **clomiphene** and tamoxifen, on mercury)

IT Pharmaceutical analysis
(polarog., of triphenylethene derivs.)

IT 569-57-3, Chlorotrianisene 911-45-5, **Clomiphene** 10540-29-1, Tamoxifen
RL: PROC (Process)
(electrochem. reduction and determination of)

IT 9004-67-5, Methyl cellulose
RL: PRP (Properties)
(polarog. reduction of triphenylethene derivs. in presence of)

L14 ANSWER 28 OF 94 MEDLINE on STN
ACCESSION NUMBER: 2004410930 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15315595
TITLE: Body fat patterning in polycystic ovary syndrome women as a predictor of the response to **clomiphene**.
AUTHOR: Douchi Tsutomu; Oki Toshimichi; Yamasaki Hideki; Nakae Mitsuhiro; Imabayashi Akiko; Nagata Yukihiro
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Faculty of Medicine, Kagoshima University, Kagoshima, Japan.
SOURCE: Acta obstetricia et gynecologica Scandinavica, (2004 Sep) Vol. 83, No. 9, pp. 838-41.
Journal code: 0370343. ISSN: 0001-6349.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200410
ENTRY DATE: Entered STN: 20040819
Last Updated on STN: 20041006
Entered Medline: 20041005

AB BACKGROUND: To investigate the difference in the response to **clomiphene** citrate (CC) based on body fat distribution in women with polycystic ovary syndrome (PCOS). METHODS: Ninety anovulatory PCOS women were divided into two subgroups based on treatment response: women who ovulated with CC (CC responders, n = 49) and those who did not ovulate with CC (CC nonresponders, n = 41). Baseline characteristics included age, age at menarche, height, weight and body mass index [BMI; weight/(height)2]. Percentage of body fat, body fat mass and the ratio of trunk fat to leg fat mass amount (trunk-leg fat ratio) were measured by dual-**energy** X-ray absorptiometry (DEXA). RESULTS: Age, age at menarche and height did not differ between the two groups. However, trunk-leg fat ratio in CC responders (0.9 +/- 0.4) was significantly lower than that in CC nonresponders (1.3 +/- 0.4) ($p < 0.001$). Percentage of body fat, body fat mass and BMI were also lower in CC responders ($p < 0.01$). On multiple regression analysis, however, trunk-leg fat ratio proved to be a superior predictor of CC responder to percentage of body fat, BMI or body fat mass (standardized regression coefficient > or = 0.510; t-values > or = 3.432; $p < 0.001$). CONCLUSIONS: Response to CC in anovulatory PCOS women differs with body fat distribution.

L14 ANSWER 29 OF 94 MEDLINE on STN
ACCESSION NUMBER: 90374877 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2118860
TITLE: Use of buserelin acetate in an in vitro fertilization program: a comparison with classical **clomiphene** citrate-human menopausal gonadotropin treatment.
AUTHOR: Lejeune B; Barlow P; Puissant F; Delvigne A; Vanrysselberge M; Leroy F
CORPORATE SOURCE: Department of Gynecology and Obstetrics, IVF Clinic, Saint-Pierre Hospital, Free University of Brussels,

Belgium.
SOURCE: Fertility and sterility, (1990 Sep) Vol. 54, No. 3, pp. 475-81.
Journal code: 0372772. ISSN: 0015-0282.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199010
ENTRY DATE: Entered STN: 19901122
Last Updated on STN: 19901122
Entered Medline: 19901016

AB A comparison has been established retrospectively between **clomiphene** citrate-human menopausal gonadotropin (CC-hMG) and buserelin acetate-hMG treatments in in vitro fertilization trials performed over a 3-year period. The analysis of 466 CC-hMG and 319 buserelin acetate-hMG trials shows that buserelin acetate-hMG stimulation generates a greater ovarian response resulting in higher numbers of oocytes being retrieved (6.2 + 3.8 versus 9.3 + 5.2) and fertilized (2.8 + 2.7 versus 4.3 + 3.8). More embryos are thus obtained, allowing a wider choice for intrauterine replacement and cryopreservation. Mean embryonic **vitality** scores do not differ (4.33 + 1.51 versus 4.44 + 1.54), implying that the embryonic quality remains similar in both treatments. A premature demise of the corpus luteum occurs in a large proportion of buserelin acetate-hMG cycles. However, when suppletive progesterone treatment is given, there is a trend toward a better implantation rate per embryo, and a significantly higher ongoing pregnancy rate is observed in relation to buserelin acetate-hMG treatment (20%) as compared with CC-hMG cycles (14%).

L14 ANSWER 30 OF 94 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:777849 CAPLUS
DOCUMENT NUMBER: 143:243261
TITLE: Impact of Induced Fit on Ligand Binding to the Androgen Receptor: A Multidimensional QSAR Study To Predict Endocrine-Disrupting Effects of Environmental Chemicals
AUTHOR(S): Lill, Markus A.; Winiger, Fabienne; Vedani, Angelo; Ernst, Beat
CORPORATE SOURCE: Institute for Molecular Pharmacy, University of Basel, Basel, CH-4056, Switz.
SOURCE: Journal of Medicinal Chemistry (2005), 48(18), 5666-5674
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors investigated the influence of induced fit of the androgen receptor binding pocket on free **energies** of ligand binding. On the basis of a novel alignment procedure using flexible docking, mol. dynamics simulations, and linear-interaction **energy** anal., the authors simulated the binding of 119 mols. representing six compound classes. The superposition of the ligand mols. emerging from the combined protocol served as input for Raptor, a receptor-modeling tool based on multidimensional QSAR allowing for ligand-dependent induced fit. Throughout the authors' study, protein flexibility was explicitly accounted for. The model converged at a cross-validated R2 = 0.858 (88 training compds.) and yielded a predictive R2 = 0.792 (26 test compds.), thereby predicting the binding affinity of all compds. close to their exptl. value. The authors then challenged the model by testing five mols. not belonging to compound classes used to train the model: the IC50 values were predicted within a factor of 4.5 compared to the exptl. data. The demonstrated predictivity of the model suggests that the authors' approach may well be beneficial for both drug discovery and the screening of environmental chems. for endocrine-disrupting effects, a problem that has recently become a cause for concern among scientists, environmental advocates, and politicians alike.

IT Chemicals

(environmental; impact of induced fit on ligand binding to the androgen receptor studied using a multidimensional QSAR study to predict endocrine-disrupting effects of environmental chems.)

IT QSAR (structure-activity relationship)
(impact of induced fit on ligand binding to the androgen receptor studied using a multidimensional QSAR study to predict endocrine-disrupting effects of environmental chems.)

IT Endocrine disrupting chemicals
RL: ADV (Adverse effect, including toxicity); PRP (Properties); BIOL (Biological study)
(impact of induced fit on ligand binding to the androgen receptor studied using a multidimensional QSAR study to predict endocrine-disrupting effects of environmental chems.)

IT Androgen receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(impact of induced fit on ligand binding to the androgen receptor studied using a multidimensional QSAR study to predict endocrine-disrupting effects of environmental chems.)

IT Simulation and Modeling
(mol. dynamics; impact of induced fit on ligand binding to the androgen receptor studied using a multidimensional QSAR study to predict endocrine-disrupting effects of environmental chems.)

IT 50-02-2, Dexamethasone 50-22-6, Corticosterone 50-23-7, Cortisol 50-24-8, Prednisolone 50-27-1, Estriol 50-28-2, Estra-1,3,5(10)-triene-3,17-diol (17β)-, biological studies 50-29-3, biological studies 52-01-7, Spironolactone 52-39-1, Aldosterone 53-19-0 53-41-8, Androsterone 53-43-0, 5,6-Didehydroisoandrosterone 53-63-4, 17-Deoxyestradiol 56-53-1, Diethylstilbestrol 57-63-6, Ethynylestradiol 57-83-0, Progesterone, biological studies 57-85-2 57-88-5, Cholesterol, biological studies 57-91-0, 17α-Estradiol 58-18-4, Methyltestosterone 58-22-0, Testosterone 58-89-9, Lindane 63-05-8, Androst-4-ene-3,17-dione 68-22-4, Norethindrone 68-23-5, Norethynodrel 71-58-9, 6α-Methyl-17α-hydroxyprogesterone acetate 72-43-5, p,p'-Methoxychlor 72-54-8 72-55-9, biological studies 76-44-8, Heptachlor 77-40-7, Bisphenol B 80-05-7, Bisphenol A, biological studies 80-46-6, 4-tert-Amylphenol 89-72-5, 2-sec-Butylphenol 92-69-3, 4-Hydroxybiphenyl 93-76-5, 2,4,5-T 94-13-3, Propylparaben 94-41-7, Chalcone 97-54-1, Isoeugenol 98-54-4, 4-tert-Butylphenol 99-71-8, 4-sec-Butylphenol 99-76-3, Methylparaben 103-16-2, 4-Benzyloxyphenol 104-40-5, 4-n-Nonylphenol 104-43-8, 4-Dodecylphenol 108-43-0, 3-Chlorophenol 115-29-7, Endosulfan 119-61-9, Benzophenone, biological studies 121-33-5, Vanillin 131-56-6, 2,4-Dihydroxybenzophenone 143-50-0, Kepone 309-00-2, Aldrin 362-05-0, 2-Hydroxyestradiol 427-51-0, Cyproterone acetate 446-72-0, Genistein 479-13-0, Coumestrol 481-30-1, Epitestosterone 487-26-3, Flavanone 520-85-4, 6α-Methyl-17α-hydroxyprogesterone 521-17-5, Androstenediol 521-18-6, 5α-Dihydrotestosterone 525-82-6, Flavone 531-95-3, Equol 552-80-7, Dimethylstilbestrol 564-35-2, 11-keto-Testosterone 571-20-0 571-22-2, 5β-Dihydrotestosterone 599-64-4, p-Cumylphenol 611-99-4, 4,4'-Dihydroxybenzophenone 659-22-3, 4,4'-Dihydroxystilbene 789-02-6 911-45-5, **Clomiphene** 965-93-5, Methyltrienolone 1057-07-4 1137-42-4, 4-Hydroxybenzophenone 1156-92-9, 4-Androstenediol 1224-92-6, 5α-Androstan-3β-ol 1225-43-0, 5α-Androstan-17β-ol 1474-53-9 1482-70-8 1570-64-5, 4-Chloro-2-methylphenol 1845-11-0, Nafoxidine 1852-53-5 2132-70-9, p,p'-Methoxychlorolefin 2529-64-8, 3-Deoxyestradiol 2657-25-2, 4'-Hydroxychalcone 2971-36-0, HPTE 3424-82-6 3704-09-4, Mibolerone 4250-77-5, 6-Hydroxyflavanone 5108-94-1 5975-78-0, Zearalanone 5976-61-4, 4-Hydroxyestradiol 6515-37-3, 4'-Hydroxyflavanone 6533-00-2, Norgestrel 6554-98-9, trans-4-Hydroxystilbene 6665-83-4, 6-Hydroxyflavone 6665-86-7, 7-Hydroxyflavone 9016-45-9, Igepal CO-210 10161-33-8, Trenbolone 10540-29-1, Tamoxifen 12789-03-6, Chlordane 13026-26-1, Hexestrol monomethyl ether 13037-86-0, 4-Heptyloxyphenol 20426-12-4, 4-Hydroxychalcone 25154-52-3, N-Nonylphenol 34184-77-5, Promegestone 36455-72-8, α-Zearalenol 42422-68-4, β-Zearalanol 68047-06-3, 4-Hydroxytamoxifen 71030-11-0, β-Zearalenol 79199-51-2, 3,3'-Dihydroxyhexestrol
RL: ADV (Adverse effect, including toxicity); PRP (Properties); BIOL

```
     (Biological study)
        (impact of induced fit on ligand binding to the androgen receptor
        studied using a multidimensional QSAR study to predict
        endocrine-disrupting effects of environmental chems.)
REFERENCE COUNT:          26    THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> s cachexia or aging or myopathies or neuromyopathy or myopathy or myasthenic syndrome or
myoglubinuria or polymyositis or myositis
L15      620699 CACHEXIA OR AGING OR MYOPATHIES OR NEUROMYOPATHY OR MYOPATHY OR
                MYASTHENIC SYNDROME OR MYOGLUBINURIA OR POLYMYOSITIS OR MYOSITIS

=> s brachial plexopathy, diabetic amyotrophy or denervation or HIV or amyotrophic lateral
sclerosis or aids
L16      707670 BRACHIAL PLEXOPATHY, DIABETIC AMYOTROPHY OR DENERVATION OR HIV
                OR AMYOTROPHIC LATERAL SCLEROSIS OR AIDS

=> s l15 or l16
L17     1319441 L15 OR L16

=> d his

     (FILE 'HOME' ENTERED AT 14:42:11 ON 01 MAR 2006)

     FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE' ENTERED AT 14:42:45 ON 01 MAR 2006
L1          1613 S 79838-56-5/RN OR 57049-00-0/RN OR 39729-47-0/RN OR 15690-57-0
L2         18503 S CLOMIPHENE OR ENCLOMIFENE OR ENCLOMIPHENE TRANS-CLOMIFENE OR
L3           299 S CIS-CLOMIPHENE OR ZUCLOMID OR ZUCLOMIPHENE
L4             6 S ENCLOMID OR TRANS-CLOMIPHEN
L5            99 S ENCLOMID OR TRANS-CLOMIPHENE
L6           300 S L3 OR CIS-CLOMIFENE
L7           359 S L3 OR ZUCLOMIFENE
L8         31489 S TESTESTERONE OR 17-HYDROXY-5ALPHA-ANDROST-1-EN-3-ONE OR 1-T
L9       3847772 S WASTING OR SLUGGISH OR MOOD OR FEELING OR ENERGY OR STAMINA O
L10          138 S L9 AND L2
L11           21 S L9 AND L7
L12            1 S L9 AND L5
L13           94 DUP REM L10 (44 DUPLICATES REMOVED)
L14           94 FOCUS L13 1-
L15       620699 S CACHEXIA OR AGING OR MYOPATHIES OR NEUROMYOPATHY OR MYOPATHY
L16       707670 S BRACHIAL PLEXOPATHY, DIABETIC AMYOTROPHY OR DENERVATION OR HI
L17      1319441 S L15 OR L16

=> s l17 and l2
L18          200 L17 AND L2

=> s l18 and l7
L19           13 L18 AND L7

=> s l18 and l5
L20            1 L18 AND L5

=> s clomiphene or enclomifene or enclomiphene or trans-clomifene or trans-clomiphene or
clomifene or clomid or chloramiphene or clomivid or clomphid
L21       18607 CLOMIPHENE OR ENCLOMIFENE OR ENCLOMIPHENE OR TRANS-CLOMIFENE OR
                TRANS-CLOMIPHENE OR CLOMIFENE OR CLOMID OR CHLORAMIPHENE OR
                CLOMIVID OR CLOMPHID

=> s l21 and l17
L22          200 L21 AND L17

=> dup rem l22
PROCESSING COMPLETED FOR L22
L23          160 DUP REM L22 (40 DUPLICATES REMOVED)

=> focus
PROCESSING COMPLETED FOR L23
L24          160 FOCUS L23 1-
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=> dup rem l19
PROCESSING COMPLETED FOR L19
L25          13 DUP REM L19 (0 DUPLICATES REMOVED)

=> focus
PROCESSING COMPLETED FOR L25
L26          13 FOCUS L25 1-

=> d ibib abs 1-13

L26  ANSWER 1 OF 13  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2004:722925  CAPLUS
DOCUMENT NUMBER:          141:218967
TITLE:                    Methods and compositions with trans-
                          clomiphene for treating wasting and
                          lipodystrophy
INVENTOR(S):              Podolski, Joseph S.; Wiehle, Ronald
PATENT ASSIGNEE(S):       Zonagen, Inc., USA
SOURCE:                   U.S. Pat. Appl. Publ., 12 pp., Cont.-in-part of U.S.
                          Ser. No. 427,768.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   3
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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     US 2004171697         A1    20040902    US 2003-712546          20031112
     WO 2003005954         A2    20030123    WO 2002-US21524         20020709
     WO 2003005954         A3    20031023
     WO 2003005954         B1    20031204
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
             CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     US 2004097597         A1    20040520    US 2003-427768          20030430
PRIORITY APPLN. INFO.:                       US 2001-304313P     P   20010709
                                             WO 2002-US21524     A2  20020709
                                             US 2003-427768      A2  20030430
AB   The invention discloses compns. and methods useful for treating wasting,
     especially a loss of muscle mass.  The present invention also discloses compns.
     and methods useful for treating lipodystrophy.  The compns. and methods of
     the present invention are particularly beneficial to HIV
     -infected individuals.

L26  ANSWER 2 OF 13  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2004:412812  CAPLUS
DOCUMENT NUMBER:          140:406808
TITLE:                    Preparation of carbonylamino-benzimidazoles as
                          selective androgen receptor modulators
INVENTOR(S):              Kim, Yuntae; Spencer, Keith L.; Hanney, Barbara;
                          Duggan, Mark E.
PATENT ASSIGNEE(S):       Merck & Co., Inc., USA
SOURCE:                   PCT Int. Appl., 136 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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| WO 2004041277 | | A1 | 20040521 | WO 2003-US34345 | 20031028 |
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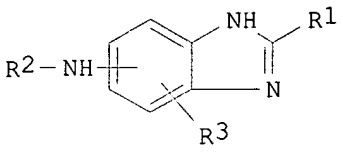
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2504044 | | AA | 20040521 | CA 2003-2504044 | 20031028 |
| EP 1581217 | | A1 | 20051005 | EP 2003-777969 | 20031028 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| US 2006036098 | | A1 | 20060216 | US 2005-533259 | 20050429 |
| PRIORITY APPLN. INFO.: | | | | US 2002-422914P | P 20021101 |
| | | | | WO 2003-US34345 | W 20031028 |

OTHER SOURCE(S): MARPAT 140:406808

GI

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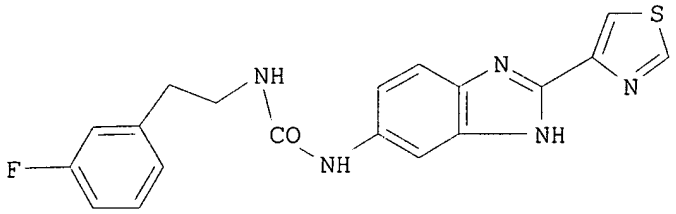



II

AB Carbonylamino-benzimidazoles (shown as I; variables defined below; e.g. II) are modulators of the androgen receptor (AR) in a tissue selective manner. They are useful as agonists of the androgen receptor in bone and/or muscle tissue while antagonizing the AR in the prostate of a male patient or in the uterus of a female patient. These compds. are therefore useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, **aging** skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, arthritic condition and joint repair, **HIV**-wasting, prostate cancer, cancer **cachexia**, Alzheimer's disease, muscular dystrophies, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents. Although the methods of preparation are not claimed, 6 example prepns. and characterization data for .apprx.150 examples of I are included; nearly all examples contain the thiazol-4-yl group at the 2 position of the benzimidazole. For example, II was prepared from 3-fluorophenethylamine, 1,1'-carbonyldiimidazole and [2-(thiazol-4-yl)-3H-benzimidazol-5-yl]amine, the latter of which was prepared from thiazole-4-carboxylic acid and (4-amino-3-nitrophenyl)carbamic acid tert-Bu ester (preparation described) via amide formation followed by cyclization in 20% aqueous AcOH. For I: R1 = aryl or heterocyclyl; R2 = -(C:O)NR5R6, -(C:O)a(C1-10)alkyl, -(C:O)a(C2-8)alkenyl, -(C:O)a(C2-8)alkynyl, -(C:O)a(C3-10)cycloalkyl, -(C:O)a(C3-8)heterocyclyl, and -(C:O)aaryl; R3 = H, halogen,

-(C:O)aOb(C1-10)alkyl, -(C:O)aOb(C2-8)alkenyl, -(C:O)aOb(C2-8)alkynyl, -(C:O)aOb(C3-10)cycloalkyl, -(C:O)aOb(C3-8)heterocyclyl, -(C:O)aObaryl, -(C:O)aNR5R6, -Ob(C:O)NR5R6, -NR5(C:O)aObRb, -NR5(C:O)NR5R6, -NR5S(O)2Rb, -(C:O)OH, trifluoromethoxy, trifluoroethoxy, -Ob(C1-10)perfluoroalkyl, -S(O)2Ob(C1-10)alkyl, -S(O)2Ob(C2-8)alkenyl, -S(O)2Ob(C2-8)alkynyl, -S(O)2Ob(C3-10)cycloalkyl, -S(O)2Ob(C3-8)heterocyclyl, -S(O)2Obaryl, -NR5S(O)2NR5R6, -CN, -NO2, oxo, and -OH; a = 0-1; b = 0-1; addnl. details are given in the claims.

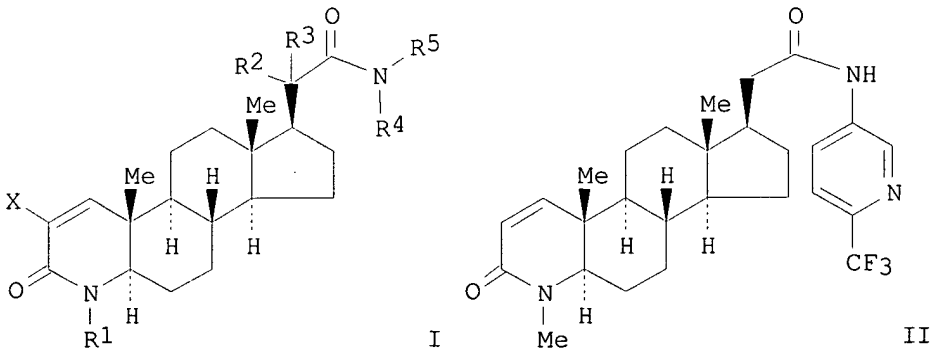
L26 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:55196 CAPLUS
DOCUMENT NUMBER: 142:156209
TITLE: Preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivatives as androgen receptor modulators
INVENTOR(S): Dankulich, William P.; Kaufman, Mildred L.; Meissner, Robert S.; Mitchell, Helen J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 158 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005005380 | A2 | 20050120 | WO 2004-US20548 | 20040625 |
| WO 2005005380 | A3 | 20050602 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-483784P P 20030630
OTHER SOURCE(S): MARPAT 142:156209
GI




AB 3-Oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs., such as I [X = H, halo; R1 = H, CF3, alkyl, alkoxy, halo, amino, alkylamino, CH2OH; R2, R3 = H, halo, alkyl, amino, aminoalkyl, alkoxyalkyl, alkoxyalkyl, alkoxycarbonylalkyl, cyano, perfluoroalkyl, alkylcarbonyl, alkylcarbonylamino; R2R3 = oxo, spirocycloalkyl; R4, R5 = H, halo, alkyl, alkenyl, alkynyl, carbonylalkyl, carbonylalkenyl, carbonylalkynyl, cycloalkyl, heterocyclyl, cycloheteroalkyl, carboxyaryl, etc.}, or a pharmaceutically acceptable salt or an enantiomer thereof, were prepared for

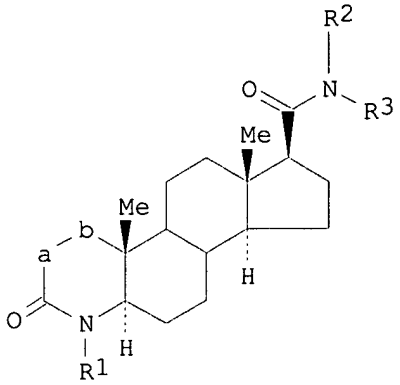
their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivative II, was prepared via a multiple step reaction sequence starting from 4-methyl-3-oxo-4-aza-5α-androst-1-ene-17-carboxylic acid and 3-amino-6-trifluoromethylpyridine. The prepared compds. are useful as agonists of the androgen receptor in bone and/or muscle tissue while antagonizing the AR in the prostate of a male patient or in the uterus of a female patient. I are therefore useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, **aging** skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, **HIV**-wasting, prostate cancer, cancer **cachexia**, Alzheimer's disease, muscular dystrophies, cognitive impairment, decreased libido, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

L26 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:757525 CAPLUS
DOCUMENT NUMBER: 139:277056
TITLE: Preparation of fluorinated 4-aza-androstan-3-one-17β-carboxamide derivatives as androgen receptor modulators
INVENTOR(S): Meissner, Robert S.; Perkins, James J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003077919 | A1 | 20030925 | WO 2003-US8277 | 20030307 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2478186 | AA | 20030925 | CA 2003-2478186 | 20030307 |
| AU 2003218235 | A1 | 20030929 | AU 2003-218235 | 20030307 |
| EP 1485095 | A1 | 20041215 | EP 2003-714228 | 20030307 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, SK | | | | |
| BR 2003008355 | A | 20050125 | BR 2003-8355 | 20030307 |
| US 2005165039 | A1 | 20050728 | US 2003-507239 | 20030307 |
| JP 2005526082 | T2 | 20050902 | JP 2003-575972 | 20030307 |
| NO 2004004312 | A | 20041012 | NO 2004-4312 | 20041012 |

PRIORITY APPLN. INFO.: US 2002-363822P P 20020313
WO 2003-US8277 W 20030307

OTHER SOURCE(S): MARPAT 139:277056
GI



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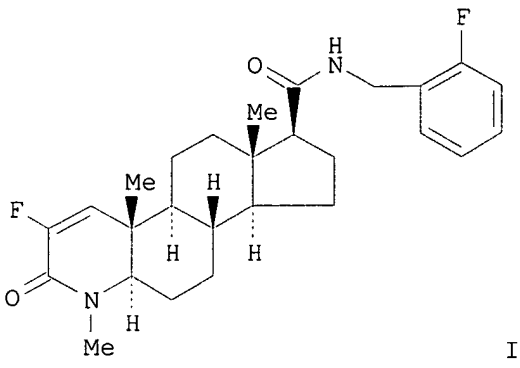

II

AB Fluorinated 4-aza-androstan-3-one-17β-carboxamide derivs., such as I [a-b = CF:CH, CHFCH2, CF2CH2; R1 = H, CH2OH, (un)substituted alkyl; R2 = H, alkyl; R3 = alkyl, cycloheteroalkyl, aryl, heteroaryl; R2R3 = 5 or 6-membered ring fused with a 5- or 6-membered aromatic ring system having 0-2 heteroatoms], or a pharmaceutically acceptable salt or an enantiomer thereof, were prepared for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, 4-aza-androstan-3-one-17β-carboxamide derivative II, was prepared via a multiple step reaction sequence starting from 4-methyl-4-aza-androstan-3-one-17-carboxylic acid Me ester and 2-fluoro-benzylamine. The prepared compds. are useful as agonists of the androgen receptor in bone and/or muscle tissue while antagonizing the AR in the prostate of a male patient or in the uterus of a female patient. I are therefore useful in the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, **aging** skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, **HIV**-wasting, prostate cancer, cancer **cachexia**, muscular dystrophies, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:259881 CAPLUS

DOCUMENT NUMBER: 142:336517

TITLE: Preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivatives for their use as modulators of the androgen receptor in a tissue selective manner

INVENTOR(S): Kaufman, Mildred L.; Meissner, Robert S.; Mitchell, Helen J.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005025572 | A1 | 20050324 | WO 2004-US28655 | 20040902 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,

AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-501789P P 20030910
OTHER SOURCE(S): MARPAT 142:336517
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB 17-Heterocyclic-4-aza-5α-androst-1-en-3-one derivs., such as I [dashed bond = single bond, double bond; X = H, halo; Y, Z = H, alkyl, halo; Y and Z, together with the carbon atom to which they are attached = cyclopropyl; n = 0-3; U, V, W, D = CH, N, S, O; R1 = H, CF3, carbonyl(alkyl), OH, alkoxy, halo, alkyl, CH2OH, alkylamino; R2 = halo, carbonyl(alkyl), carbonyl(alkenyl), carbonyl(alkynyl), alkenylamino, heterocyclic, etc.], were prepared for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, II (R = OH) was treated with Et3N, and iso-Bu chloroformate, followed by reaction with N,O-dimethylhydroxylamine hydrochloride to give II [R = N(Me)OMe (III)]. III was converted to 4-aza-5α-androst-1-en-3,20-dione derivative II (R = Me), and then to bromide II [R = CH2Br (IV)], which was treated with N-butyl-thiourea to afford V. The prepared compds. are useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, **aging** skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, **HIV**-wasting, prostate cancer, benign prostatic hyperplasia (BPH), abdominal adiposity, metabolic syndrome, type II diabetes, cancer **cachexia**, Alzheimer's disease, muscular dystrophies, cognitive decline, sexual dysfunction, sleep apnea, depression, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:58320 CAPLUS
DOCUMENT NUMBER: 142:156210
TITLE: Preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivatives as androgen receptor modulators
INVENTOR(S): Dankulich, William P.; Kaufman, Mildred L.; Meissner, Robert S.; Mitchell, Helen J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005005606 | A2 | 20050120 | WO 2004-US20539 | 20040625 |
| WO 2005005606 | A3 | 20050602 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-483675P P 20030630

OTHER SOURCE(S): MARPAT 142:156210

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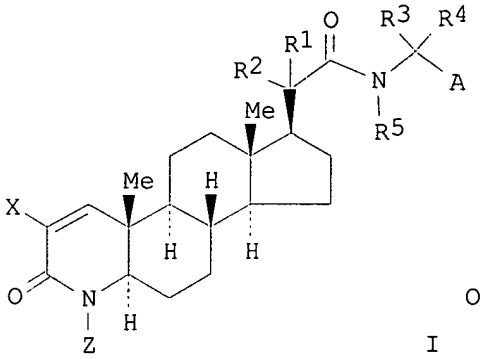


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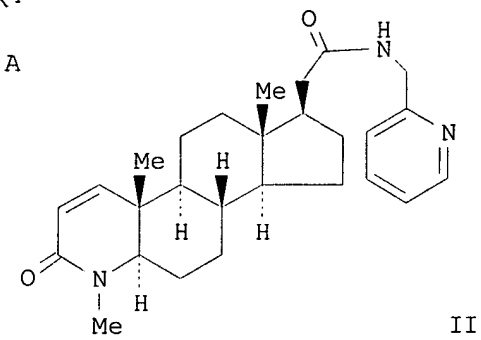


II

AB 3-Oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs., such as I [X = H, halo; Z = H, CF3, carbonylalkyl, alkyl, alkoxy, halo, CH2OH; A = aromatic ring having 0-4 heteroatoms; polycyclic ring system having one or more aromatic rings and 0-4 heteroatoms; R1, R2, R3, R4, R5 = H, halo, alkyl, amino, alkylamino, aminoalkyl, alkoxyalkyl, alkoxyalkyl, alkoxycarbonylalkyl, cyano, perfluoroalkyl, alkylcarbonyl, alkylcarbonylamino, etc.; R1R2, R3R4 = oxo, spirocycloalkyl], or a pharmaceutically acceptable salt or an enantiomer thereof, were prepared for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivative II, was prepared via a multiple step reaction sequence starting from 4-methyl-3-oxo-4-aza-5α-androst-1-ene-17-carboxylic acid and 2-aminomethylpyridine. I are therefore useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, **aging** skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, **HIV**-wasting, prostate cancer, benign prostatic hyperplasia (BPH), cancer **cachexia**, Alzheimer's disease, muscular dystrophies, cognitive decline, sexual dysfunction, sleep apnea, depression, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

L26 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:259887 CAPLUS

DOCUMENT NUMBER: 142:336518

TITLE: Preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivatives as androgen receptor modulators

INVENTOR(S): Meissner, Robert S.; Mitchell, Helen J.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| WO 2005025579 | A1 | 20050324 | WO 2004-US28641 | 20040902 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-501664P P 20030910
OTHER SOURCE(S): MARPAT 142:336518
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention discloses preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs., such as I [dashed bond = single bond, double bond; X = H, halo; Y, Z = H, alkyl, halo; Y and Z, together with the carbon atom to which they are attached = cyclopropyl; n = 0-3; U, V, W, D = CH, N, provided that at least U, V, W, and D = CH; R1 = H, CF3, carbonyl(alkyl), OH, alkoxy, halo, alkyl, CH2OH, alkylamino; R2 = halo, carbonyl(alkyl), carbonyl(alkenyl), carbonyl(alkynyl), alkenylamino, heterocyclic, etc.], for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, 4-azaandrost-1-ene derivative II was reacted with 2,3-diaminopyridine in presence of silver triflate to give 17β-carboxamide derivative III, which, on heating with polyphosphoric acid, afforded 17β-imidazopyridinyl-3-oxo-4-aza-5α-androst-1-ene derivative IV. I are therefore useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, **aging** skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, **HIV**-wasting, prostate cancer, benign prostatic hyperplasia (BPH), abdominal adiposity, metabolic syndrome, type II diabetes, cancer **cachexia**, Alzheimer's disease, muscular dystrophies, cognitive decline, sexual dysfunction, sleep apnea, depression, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:892539 CAPLUS
DOCUMENT NUMBER: 139:375605
TITLE: Synthesis and uses of 4-azasteroid derivatives as selective androgen receptor modulators (SARMs)
INVENTOR(S): Wang, Jiabing; McVean, Carol A.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 181 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003092588 | A2 | 20031113 | WO 2003-US13120 | 20030425 |
| WO 2003092588 | A3 | 20040715 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | | |
|---|---|---|---|---|---|
| CA 2484173 | AA | 20031113 | CA 2003-2484173 | | 20030425 |
| EP 1501512 | A2 | 20050202 | EP 2003-719957 | | 20030425 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | | |
| US 2005131005 | A1 | 20050616 | US 2003-512800 | | 20030425 |
| JP 2005529897 | T2 | 20051006 | JP 2004-500773 | | 20030425 |
| PRIORITY APPLN. INFO.: | | | US 2002-376779P | P | 20020430 |
| | | | WO 2003-US13120 | W | 20030425 |

OTHER SOURCE(S): MARPAT 139:375605

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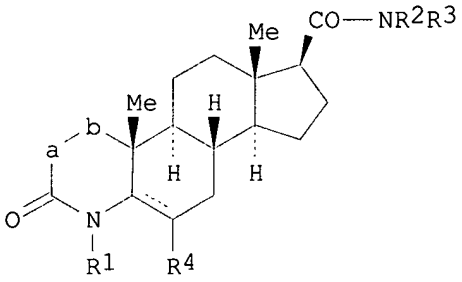



AB Compds. of structural formula (I) are modulators of the androgen receptor (AR) in a tissue selective manner. They are useful as agonists of the androgen receptor in bone and/or muscle tissue while antagonizing the AR in the prostate of a male patient or in the uterus of a female patient. These compds. are therefore useful in the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, **aging** skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, **HIV**-wasting, prostate cancer, cancer **cachexia**, Alzheimer's disease, muscular dystrophies, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

L26 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:261603 CAPLUS
DOCUMENT NUMBER: 138:281598
TITLE: Androstane compounds as androgen receptor (AR) modulators for the treatment of AR-related diseases
INVENTOR(S): Wang, Jiabing
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003026568 | A2 | 20030403 | WO 2002-US29436 | 20020917 |
| WO 2003026568 | A3 | 20040226 | | |

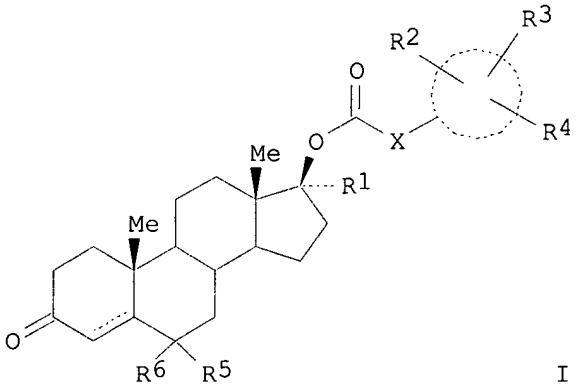
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| CA 2459943 | AA | 20030403 | CA 2002-2459943 | 20020917 |
| EP 1429779 | A2 | 20040623 | EP 2002-766288 | 20020917 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| JP 2005507886 | T2 | 20050324 | JP 2003-530207 | 20020917 |
| US 2004235808 | A1 | 20041125 | US 2004-489072 | 20040308 |
| PRIORITY APPLN. INFO.: | | | US 2001-324124P | P 20010921 |
| | | | WO 2002-US29436 | W 20020917 |

OTHER SOURCE(S): MARPAT 138:281598

GI




I

AB Compds. of structural formula (I) as herein defined are claimed as useful in a method for modulating a function of the androgen receptor in a tissue selective manner in a patient in need of such modulation, as well as in a method of activating the function of the androgen receptor in a patient, and in particular the method wherein the function of the androgen receptor is blocked in the prostate of a male patient or in the uterus of a female patient and activated in bone and/or muscle tissue. These compds. are useful in the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteopenia, osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, **aging** skin, male hypogonadism, female sexual dysfunction, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, aplastic anemia and other hematopoietic disorders, pancreatic cancer, renal cancer, prostate cancer, inflammatory arthritis and joint repair, alone or in combination with other active agents. Methods for the co-administration of those compds. with bone-strengthening agents are also claimed.

L26 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1311659 CAPLUS

DOCUMENT NUMBER: 144:51330

TITLE: N-benzyl-2-phenylbutanamides as tissue-selective androgen receptor modulators, their preparation, pharmaceutical compositions, and use in therapy

INVENTOR(S): Hanney, Barbara; Kim, Yuntae; Krout, Michael R.; Meissner, Robert S.; Mitchell, Helen J.; Musselman, Jeffrey; Perkins, James J.; Wang, Jiabing

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 50 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

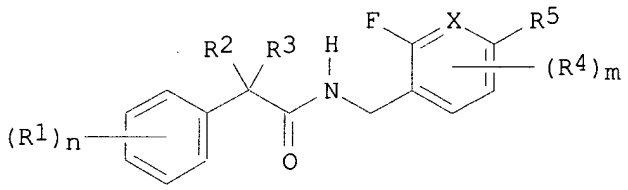
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2005277681 | A1 | 20051215 | US 2005-145490 | 20050603 |
| WO 2005120477 | A2 | 20051222 | WO 2005-US19554 | 20050603 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

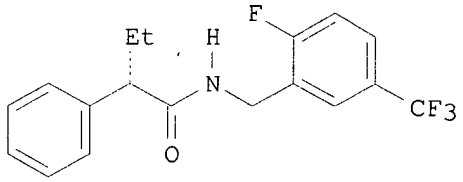
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-577698P P 20040607

GI




I




II

AB The invention relates to compds. of structural formula I, which are modulators of the androgen receptor (AR) in a tissue-selective manner. In compds. I, X is CH or N; n is 0, 1, 2, or 3; m is 0, 1, or 2; R1, R4, and R5 are independently selected from H, halo, cyano, (un)substituted C1-10 alkyl, (un)substituted C2-10 alkenyl, (un)substituted aryl-C0-10 alkyl, (un)substituted perfluoro-C1-6 alkyl, etc.; R2 and R3 are independently selected from H, halo, cyano, amino, hydroxy-C0-10 alkyl, (un)substituted C1-10 alkyl, (un)substituted C2-10 alkenyl, (un)substituted aryl-C0-10 alkyl, (un)substituted perfluoro-C1-6 alkyl, etc. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of a compound I and a pharmaceutically acceptable carrier, as well as to the use of the compns. for the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration. Coupling of (S)-2-phenylbutanoic acid with 2-fluoro-5-(trifluoromethyl)benzylamine gave butanamide II. Compds. of the invention, e.g., II, express affinity for endogenously expressed androgen receptor with IC50 values of 1 μM or less.

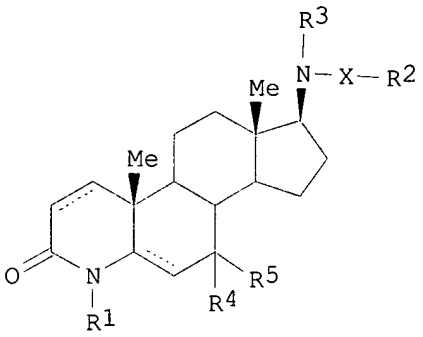
L26 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:1015853 CAPLUS
DOCUMENT NUMBER: 142:1359
TITLE: Identification and synthesis of androgen receptor modulators and therapeutic uses thereof
INVENTOR(S): Meissner, Robert S.; Perkins, James J.

PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 165 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004100874 | A2 | 20041125 | WO 2004-US13787 | 20040503 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2524409 | AA | 20041125 | CA 2004-2524409 | 20040503 |
| EP 1622567 | A2 | 20060208 | EP 2004-751257 | 20040503 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | | |

PRIORITY APPLN. INFO.: US 2003-468579P P 20030507
WO 2004-US13787 W 20040503

OTHER SOURCE(S): MARPAT 142:1359
GI




I

AB Compds. of structural formula (I) as herein defined are disclosed as useful in a method for modulating the androgen receptor in a tissue selective manner in a patient in need of such modulation, as well as in a method of agonizing the androgen receptor in a patient, and in particular the method wherein the androgen receptor is antagonized in the prostate of a male patient or in the uterus of a female patient and agonized in bone and/or muscle tissue. Method for the synthesis of those compds., as well as techniques for the screening of androgen receptor modulation capacity of those compds. are exemplified. These compds. are useful in the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including: osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, **aging** skin, male hypogonadism, post-menopausal symptoms in women, female sexual dysfunction, atherosclerosis, hypercholesterolemia, hyperlipidemia, aplastic anemia and other hematopoietic disorders, pancreatic cancer, renal cancer, arthritis and joint repair, alone or in combination with other active agents. In addition, these compds. are useful as pharmaceutical composition ingredients alone and in combination with other active agents.

L26 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:55024 CAPLUS

DOCUMENT NUMBER: 142:134783
TITLE: 17-Acetamido-4-azasteroid derivatives as androgen receptor modulators for the treatment of related diseases
INVENTOR(S): Dankulich, William P.; Meissner, Robert S.; Mitchell, Helen J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005004807 | A2 | 20050120 | WO 2004-US20753 | 20040625 |
| WO 2005004807 | A3 | 20050407 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-483664P P 20030630
OTHER SOURCE(S): MARPAT 142:134783
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB 17-Acetamido-4-azasteroid derivs., I (X = H or halogen; R1 = H, CF3, CO, C1-3 alkyl, C1-4 alkoxy, halogen , hydroxymethyl, wherein said alkyl, and alkoxy are optionally substituted with 1-7 F atoms; Y = a substituted or unsubstituted hetercycle containing at least one nitrogen; R2, R3 = H, halogen, C1-8 alkyl, aminoalkyl, hydroxycarbonyl, CN, OH, etc.) were prepared as androgen receptor modulators for the treatment of related diseases. Thus, II was treated with Et3N, and iso-Bu chloroformate, followed by LiBH4 to give the alchol. This alc. was converted to the tosylate, which was converted to the nitrile. Oxidation of the nitrile resulted in formation of the corresponding acid which was treated with 2-oxopiperizine, EDC, and HOAt to give III.

L26 ANSWER 13 OF 13 MEDLINE on STN
ACCESSION NUMBER: 77209022 MEDLINE
DOCUMENT NUMBER: PubMed ID: 874494
TITLE: Effect of **zuclomiphene** on cholesterol formation in the developing central nervous system of the rat.
AUTHOR: Ramsey R B; Fredericks M; Fischer V W
SOURCE: Journal of neurochemistry, (1977 Jun) Vol. 28, No. 6, pp. 1317-21.
Journal code: 2985190R. ISSN: 0022-3042.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197708
ENTRY DATE: Entered STN: 19900314
Last Updated on STN: 19900314
Entered Medline: 19770825

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L2         18503 S CLOMIPHENE OR ENCLOMIFENE OR ENCLOMIPHENE TRANS-CLOMIFENE OR
L3           299 S CIS-CLOMIPHENE OR ZUCLOMID OR ZUCLOMIPHENE
L4             6 S ENCLOMID OR TRANS-CLOMIPHEN
L5            99 S ENCLOMID OR TRANS-CLOMIPHENE
L6           300 S L3 OR CIS-CLOMIFENE
L7           359 S L3 OR ZUCLOMIFENE
L8         31489 S TESTESTERONE OR 17-HYDROXY-5ALPHA-ANDROST-1-EN-3-ONE OR 1-T
L9       3847772 S WASTING OR SLUGGISH OR MOOD OR FEELING OR ENERGY OR STAMINA O
L10          138 S L9 AND L2
L11           21 S L9 AND L7
L12            1 S L9 AND L5
L13           94 DUP REM L10 (44 DUPLICATES REMOVED)
L14           94 FOCUS L13 1-
L15       620699 S CACHEXIA OR AGING OR MYOPATHIES OR NEUROMYOPATHY OR MYOPATHY
L16       707670 S BRACHIAL PLEXOPATHY, DIABETIC AMYOTROPHY OR DENERVATION OR HI
L17      1319441 S L15 OR L16
L18          200 S L17 AND L2
L19           13 S L18 AND L7
L20            1 S L18 AND L5
L21        18607 S CLOMIPHENE OR ENCLOMIFENE OR ENCLOMIPHENE OR TRANS-CLOMIFENE
L22          200 S L21 AND L17
L23          160 DUP REM L22 (40 DUPLICATES REMOVED)
L24          160 FOCUS L23 1-
L25           13 DUP REM L19 (0 DUPLICATES REMOVED)
L26           13 FOCUS L25 1-

=> d ibib abs it l23 1-30

L23  ANSWER 1 OF 160  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:        2006:100738  CAPLUS
TITLE:                   Novel dosage form comprising modified-release and
                         immediate-release active ingredients
INVENTOR(S):             Vaya, Navin; Karan, Rajesh Singh; Sadanand, Sunil;
                         Gupta, Vinod Kumar
PATENT ASSIGNEE(S):      India
SOURCE:                  U.S. Pat. Appl. Publ., 49 pp., Cont.-in-part of U.S.
                         Ser. No. 630,446.
                         CODEN: USXXCO
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  2
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.          DATE
     --------------      ----   --------    --------------------     --------
     US 2006024365        A1    20060202    US 2005-134633           20050519
     US 2004096499        A1    20040520    US 2003-630446           20030729
PRIORITY APPLN. INFO.:                      IN 2002-MU697       A    20020805
                                            IN 2002-MU699       A    20020805
                                            IN 2003-MU80        A    20030122
                                            IN 2003-MU82        A    20030122
                                            US 2003-630446      A2   20030729
AB   A dosage form comprising of a high dose, high solubility active ingredient as
     modified release and a low dose active ingredient as immediate release
     where the weight ratio of immediate release active ingredient and modified
     release active ingredient is from 1:10 to 1:15000 and the weight of modified
     release active ingredient per unit is from 500 mg to 1500 mg; a process
     for preparing the dosage form.  Tablets containing 10 mg sodium pravastatin and
     1000 mg niacin were prepared  The release of sodium pravastatin after 24 h
     was 67.7%, and the release of niacin after 1 h was 84.1%.
IT   tRNA
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (2-(diethylamino)ethanol complexes; novel dosage form comprising
```

modified-release and immediate-release active ingredients)
IT Fatty acids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C14-18, C14-18-alkyl esters; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Alcohols
Glycerides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C16-18; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Antihistamines
(H2; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Histamine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(H2; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Canarypox virus
(IL-2; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Natural products, pharmaceutical
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Kutkin; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Glutamate antagonists
(NMDA antagonists; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Bone, disease
(Paget's, drugs for treatment of; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Monoglycerides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(acetates; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Estrogen receptors
Estrogens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonists; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Nervous system, disease
(**amyotrophic lateral sclerosis**, drugs for treatment of; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Hormones, animal
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anabolic steroids; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Polyamines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(analogs; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Heart, disease
(angina pectoris, unstable, drugs for treatment of; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Antirheumatic agents
(antagonist; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Antiarteriosclerotics
(antiatherosclerotics; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Antitumor agents
(antineoplastons; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Natural products, pharmaceutical
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(belladonna; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Enzymes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cell-lytic; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Ischemia, disease
(cerebral, drugs for treatment of; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Porphyrins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chlorins, benzo-; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Porphyrins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chlorins; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Tannins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compds. with 8-L-argininevasopressin; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Estrogens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugated; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Quinones
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclopentanthraquinones; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Natural products, pharmaceutical
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(digitalis; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Gastrointestinal motility
(effectors; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Fatty acids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(esters; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Placenta
(extract, Laennec; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Rhus diversiloba
(extract; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Alcohols
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fatty; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(follicle regulatory; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Hair preparations
(growth stimulants; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Mucopolysaccharides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heparinoids; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Castor oil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrogenated; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Peptides
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(immunostimulant; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Acne
Bone resorption inhibitors
Cartilage
Signal transduction, biological

Thyroid gland
Translation, genetic
Ulcer
(inhibitors; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Gastric acid
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Brain, disease
(ischemia, drugs for treatment of; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Gonadotropins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(memopausal; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Hydrocarbon waxes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microcryst.; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Double stranded RNA
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mismatched; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mumps skin test; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Eye
Nervous system agents
(mydriatics; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Decongestants
(nasal; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Cytoprotective agents
(neuroprotective; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Agranulocytosis
(neutropenia, inhibitors; novel dosage form comprising modified-release and immediate-release active ingredients)

IT 5-HT antagonists
Adrenoceptor agonists
Adrenoceptor antagonists
Allergy inhibitors
Analgesics
Anesthetics
Angiogenesis inhibitors
Antiandrogens
Antianginal agents
Antiarthritics
Antiasthmatics
Anticholesteremic agents
Anticoagulants
Antidiabetic agents
Antiemetics
Antiestrogens
Antihypertensives
Antioxidants
Antitumor agents
Antiviral agents
Appetite depressants
Beeswax
Bronchodilators
Cholinergic agonists
Cytotoxic agents
Diphtheria
Diuretics
Dopamine agonists

Expectorants
Fibrinolytics
Hemostatics
Hypnotics and Sedatives
Hypolipemic agents
Imaging agents
Immunomodulators
Immunostimulants
Immunosuppressants
Nervous system stimulants
Neuromuscular blocking agents
Ozocerite
Parasiticides
Pituitary gland
Platelet aggregation inhibitors
Psychotropics
Radical scavengers
Radioactive substances
Rauvolfia serpentina
Tranquilizers
Vasoconstrictors
Vasodilators
Wound healing
(novel dosage form comprising modified-release and immediate-release active ingredients)

IT Acrylic polymers
Amino acids
Antisense oligonucleotides
Carnauba wax
Corticosteroids
Estrogens
Fibrinogens
Glucocorticoids
Gonadotropins
Hormones, animal
Interferons
Interleukins
Neuregulin 1
Oligonucleotides
Pentosans
Ribozymes
Stem cell factor
Steroids
Taxanes
Thyroid hormones
Tuberculin
Waxes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release active ingredients)

IT Proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reticulon; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Oligonucleotides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sense; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Muscle relaxants
(spasmolytics; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Protamines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sulfates; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Glycosaminoglycans
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthetic; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Drug delivery systems
(tablets, compressed; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Drug delivery systems
(tablets, immediate release; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Drug delivery systems
(tablets, sustained-release; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Drug delivery systems
(tablets; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Dyes
(tellurapyrylium; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(trichohyalins; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Cytotoxic agents
(tyrphostins; novel dosage form comprising modified-release and immediate-release active ingredients)
IT 249886-47-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CLX 0921; novel dosage form comprising modified-release and immediate-release active ingredients)
IT 151763-64-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Capromab; novel dosage form comprising modified-release and immediate-release active ingredients)
IT 9034-40-6, LHRH
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(agonists; novel dosage form comprising modified-release and immediate-release active ingredients)
IT 52-39-1, Aldosterone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonist; novel dosage form comprising modified-release and immediate-release active ingredients)
IT 65154-06-5, Platelet activating factor
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antagonists; novel dosage form comprising modified-release and immediate-release active ingredients)
IT 50-99-7, D-Glucose
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(blood, regulators; novel dosage form comprising modified-release and immediate-release active ingredients)
IT 676559-96-9, Aethacizin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ethacizin; novel dosage form comprising modified-release and immediate-release active ingredients)
IT 50-67-9, Serotonin 70-18-8, Glutathione 9040-48-6, Gelatinase 52660-18-1, Casein kinase 79955-99-0, Stromelysin 120178-12-3, Telomerase 141256-52-2, Matrilysin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; novel dosage form comprising modified-release and immediate-release active ingredients)
IT 9002-17-9, Xanthine oxidase 9013-05-2, Phosphatase 106096-93-9, Bfgf
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors; novel dosage form comprising modified-release and immediate-release active ingredients)
IT 50-02-2, Dexamethasone 50-04-4, Cortisone acetate 50-06-6, Phenobarbital 50-12-4, Mephenytoin 50-13-5, Meperidine hydrochloride 50-18-0, Cyclophosphamide 50-19-1, Hydroxyphenamate 50-23-7, Hydrocortisone 50-24-8, Prednisolone 50-27-1, Estriol 50-28-2, Estra-1,3,5(10)-triene-3,17-diol (17β)- 50-33-9, Phenylbutazone 50-34-0, Propantheline bromide 50-35-1, Thalidomide 50-36-2, Cocaine 50-52-2, Thioridazine 50-53-3, Chlorpromazine 50-55-5, Reserpine 50-56-6, Oxytocin 50-57-7, Lypressin 50-58-8, Phendimetrazine tartrate 50-59-9, Cephaloridine 50-65-7, Niclosamide 50-76-0, Dactinomycin

50-78-2, Aspirin 50-91-9, Floxuridine 51-05-8, Procaine hydrochloride 51-15-0, Pralidoxime chloride 51-21-8, Fluorouracil 51-30-9, Isoproterenol hydrochloride 51-40-1, Norepinephrine bitartrate 51-43-4, Epinephrine 51-52-5, Propylthiouracil 51-55-8, Atropine 51-56-9, Homatropine hydrobromide 51-57-0, Methamphetamine hydrochloride 51-64-9, Dextroamphetamine 51-83-2, Carbachol 52-01-7, Spironolactone 52-24-4, Thiotepa 52-49-3, Trihexyphenidyl hydrochloride 52-68-6, Metrifonate 52-76-6, Lynestrenol 52-86-8, Haloperidol 52-88-0, Methylatropine nitrate 52-89-1, Cysteine hydrochloride 53-03-2, Prednisone 53-16-7D, Estrone, esters 53-19-0, Mitotane 53-34-9, Fluprednisolone 53-39-4, Oxandrolone 53-43-0, Dehydroepiandrosterone 53-60-1, Promazine hydrochloride 53-73-6, Angiotensin amide 53-79-2, Puromycin 53-84-9, Nadide 53-86-1, Indometacin 54-03-5, Hexobendine 54-05-7, Chloroquine 54-21-7, Sodium salicylate 54-31-9, Furosemide 54-35-3, Penicillingprocaine 54-36-4, Metyrapone 54-42-2, Idoxuridine 54-64-8, Thimerosal 54-84-2, Cinanserin hydrochloride 54-85-3, Isoniazid 54-91-1, Pipobroman 55-03-8, Levothyroxine sodium 55-06-1, Liothyronine sodium 55-63-0, Nitroglycerin 55-86-7, Mechlorethamine hydrochloride 55-91-4, Isoflurophate 55-98-1, Busulfan 56-45-1, Serine 56-47-3, Desoxycorticosterone acetate 56-53-1, Diethylstilbestrol 56-59-7, Felypressin 56-75-7, Chloramphenicol 56-84-8, Aspartic acid 56-87-1, Lysine 56-89-3, Cystine 56-94-0, Demecarium bromide 57-13-6, Urea 57-41-0, Phenytoin 57-47-6, Physostigmine 57-53-4, Meprobamate 57-63-6, Ethinyl estradiol 57-65-8, Thyromedan hydrochloride 57-66-9, Probenecid 57-68-1, Sulfamethazine 57-83-0, Progesterone 57-91-0, 17-α Estradiol 57-94-3, Tubocurarine chloride 57-96-5, Sulfinpyrazone 58-08-2, Caffeine 58-14-0, Pyrimethamine 58-18-4, Methyltestosterone 58-22-0, Testosterone 58-25-3, Chlordiazepoxide 58-28-6, Desipramine hydrochloride 58-32-2, Dipyridamole 58-33-3, Promethazine hydrochloride 58-38-8, Prochlorperazine 58-39-9, Perphenazine 58-54-8, Ethacrynic acid 58-55-9, Theophylline 58-71-9, Cephalothin sodium 58-86-6, Xylose 58-93-5, Hydrochlorothiazide 58-94-6, Chlorothiazide 59-05-2, Methotrexate 59-30-3, Folic acid 59-33-6, Pyrilamine maleate 59-52-9, Dimercaprol 59-63-2, Isocarboxazid 59-67-6, Niacin 59-87-0, Nitrofurazone 59-92-7, Levodopa 59-97-2, Tolazoline hydrochloride 60-13-9, Amphetamine sulfate 60-18-4, Tyrosine 60-23-1, Cysteamine 60-29-7, Ether 60-45-7, Fenimide 60-54-8, Tetracycline 60-56-0, Methimazole 60-80-0, Antipyrine 60-99-1, Methotrimeprazine 61-25-6, Papaverine hydrochloride 61-56-3, Sulthiame 61-57-4, Niridazole 61-68-7, Mefenamic acid 61-73-4, Methylene blue 61-75-6, Bretylium tosylate 61-76-7, Phenylephrine hydrochloride 61-90-5, Leucine 62-51-1, Methacholine chloride 62-68-0, Proadifen hydrochloride 62-73-7, Dichlorvos 62-90-8, Nandrolone phenpropionate 63-05-8, Androstenedione 63-12-7, Benzquinamide 63-39-8, Uridine triphosphate 63-45-6, Primaquine phosphate 63-68-3, Methionine 63-89-8, Colfosceril palmitate 63-91-2, Phenylalanine 63-92-3, Phenoxybenzamine hydrochloride 63-98-9, Phenacemide 64-31-3, Morphine sulfate 64-43-7, Amobarbital sodium 64-55-1, Mebutamate 64-77-7, Tolbutamide 64-86-8, Colchicine 65-28-1, Phentolamine mesylate 65-29-2, Gallamine triethiodide 65-45-2, Salicylamide 66-75-1, Uracil mustard 66-76-2, Dicumarol 66-81-9, Cycloheximide 67-20-9, Nitrofurantoin 67-43-6, Pentetic acid 67-45-8, Furazolidone 67-63-0, Isopropyl alcohol 67-68-5, Dimethyl sulfoxide 67-73-2, Fluocinolone acetonide 67-92-5, Dicyclomine hydrochloride 67-95-8, Quingestrone 67-96-9, Dihydrotachysterol 68-22-4, Norethindrone 68-23-5, Norethynodrel 68-35-9, Sulfadiazine 68-41-7, Cycloserine 68-89-3, Dipyrone 68-91-7, Trimethaphan camsylate 68-96-2, 17 hydroxy progesterone 69-44-3, Amodiaquine hydrochloride 69-53-4, Ampicillin 69-57-8, Penicillingsodium 69-65-8, Mannitol 69-72-7, Salicylic acid 69-74-9, Cytarabine hydrochloride 70-00-8, Trifluridine 70-10-0, Ticlatone 70-30-4, Hexachlorophene 71-00-1, Histidine 71-27-2, Succinylcholine chloride 71-58-9, Medroxyprogesterone acetate 71-63-6, Digitoxin 71-68-1, Hydromorphone hydrochloride 71-73-8, Thiopental sodium 71-81-8, Isopropamide iodide 72-18-4, Valine 72-19-5, Threonine 72-33-3, Mestranol 72-44-6, Methaqualone 73-09-6, Etozolin 73-22-3, Tryptophan 73-31-4, Melatonin 73-32-5, Isoleucine 73-48-3, Bendroflumethiazide 74-79-3, Arginine 75-00-3, Ethyl chloride 75-19-4, Cyclopropane 76-38-0,

Methoxyflurane 76-42-6, Oxycodone 76-43-7, Fluoxymesterone 76-57-3, Codeine 76-73-3, Secobarbital 76-74-4, Pentobarbital 76-90-4, Mepenzolate bromide 77-21-4, Glutethimide 77-26-9, Butalbital 77-27-0, Thiamylal 77-36-1, Chlorthalidone 77-41-8, Methsuximide 77-46-3, Acedapsone 77-67-8, Ethosuximide 77-86-1, Trometamol 78-11-5, Pentaerythritol tetranitrate 78-44-4, Carisoprodol 79-09-4, Propionic acid 79-17-4, Pimagedine 79-57-2, Oxytetracycline 79-64-1, Dimethisterone 80-08-0, Dapsone 80-50-2, Anisotropine methylbromide 81-04-9, 1,5-Naphthalenedisulfonic acid 81-13-0, Dexpanthenol 81-23-2, Dehydrocholic acid 81-54-9, Purpurin 82-92-8, Cyclizine 83-43-2, Methylprednisolone 83-73-8, Iodoquinol 83-74-9, Ibogaine 84-17-3, Dienestrol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release active ingredients)

IT 85-79-0, Dibucaine 86-13-5, Benztropine 86-34-0, Phensuximide 86-35-1, Ethotoin 86-42-0, Amodiaquine 87-08-1, Penicillin V 87-90-1, Symclosene 89-25-8, Edaravone 89-57-6, Mesalamine 90-01-7, Salicyl alcohol 90-03-9, Mercufenol chloride 90-33-5, Hymecromone 90-86-8, Cinnamedrine 91-33-8, Benzthiazide 92-13-7, Pilocarpine 93-23-2, Lauryl isoquinolinium bromide 94-09-7, Benzocaine 94-12-2, Risocaine 94-14-4, Isobutamben 94-20-2, Chloropropamide 94-24-6, Tetracaine 94-25-7, Butamben 94-36-0, Benzoyl peroxide 95-25-0, Chlorzoxazone 96-82-2 96-83-3, Iopanoic acid 97-24-5, Fenticlor 97-53-0, Eugenol 97-77-8, Disulfiram 98-72-6, Nitarsone 98-96-4, Pyrazinamide 99-66-1, Valproic acid 99-79-6, Iophendylate 100-33-4, Pentamidine 100-55-0, Nicotinyl alcohol 100-97-0, Methenamine 101-26-8, Pyridostigmine bromide 101-31-5, Hyoscyamine 101-40-6, Propylhexedrine 102-71-6, Trolamine 102-76-1, Triacetin 103-90-2, Paracetamol 104-31-4, Benzonatate 106-48-9 108-46-3, Resorcinol 110-85-0, Piperazine 112-24-3, Trientine 112-38-9, Undecylenic acid 112-72-1, 1-Tetradecanol 112-92-5, Stearyl [alcohol;] 113-18-8, Ethchlorvynol 113-52-0, Imipramine hydrochloride 113-59-7, Chlorprothixene 113-79-1D, Argipressin, hcompds. with tannate 113-92-8, Chlorpheniramine maleate 113-98-4, Penicillingpotassium 114-07-8, Erythromycin 114-49-8, Scopolamine hydrobromide 114-70-5, Sodium phenylacetate 114-80-7, Neostigmine bromide 114-85-2, Bethanidine sulfate 114-86-3, Phenformin 114-90-9, Obidoxime chloride 115-02-6, Azaserine 115-38-8, Mephobarbital 116-38-1, Edrophonium chloride 117-96-4, Diatrizoic acid 118-68-3, Etryptamine acetate 120-29-6D, Tropine, esters 120-97-8, Dichlorphenamide 121-19-7, Roxarsone 121-54-0, Benzethonium chloride 121-81-3, Nitromide 122-09-8, Phentermine 122-16-7, Sulfanitran 122-18-9, Cetalkonium chloride 122-32-7D, Triolein, iodo derivs., iodine-125 and iodine 131 122-79-2, Phenylacetate 123-03-5, Cetylpyridinium chloride 123-63-7, Paraldehyde 123-99-9, Azelaic acid 124-07-2, Octanoic acid 124-43-6, Carbamide peroxide 124-72-1, Teflurane 124-94-7, Triamcinolone 125-33-7, Primidone 125-40-6, Butabarbital 125-45-1, Azetepa 125-71-3, Dextromethorphan 125-72-4, Levorphanol tartrate 126-07-8, Griseofulvin 126-22-7, Butonate 126-27-2, Oxethazaine 127-07-1, Hydroxyurea 127-33-3, Demeclocycline 127-48-0, Trimethadione 127-69-5, Sulfisoxazole 127-71-9, Sulfabenzamide 127-77-5, Sulfabenz 127-79-7, Sulfamerazine 128-13-2, Ursodiol 128-62-1, Noscapine 129-06-6, Coumadin 129-20-4, Oxyphenbutazone 129-49-7, Methysergide maleate 129-51-1, Ergonovine maleate 129-74-8, Buclizine hydrochloride 130-16-5, Cloxyquin 130-26-7, Clioquinol 130-81-4, Quindonium bromide 131-49-7, Diatrizoate meglumine 132-17-2, Benztropine mesylate 132-35-4, Proxazole citrate 132-65-0, Dibenzothiophene 132-69-4, Benzydamine hydrochloride 132-92-3, Methicillin sodium 132-98-9, Penicillinvpotassium 133-11-9, Phenyl aminosalicylate 133-58-4, Nitromersol 133-67-5, Trichlormethiazide 134-80-5, Diethylpropion hydrochloride 135-07-9, Methyclothiazide 135-09-1, Hydroflumethiazide 136-40-3, Phenazopyridine hydrochloride 136-77-6, Hexylresorcinol 137-26-8, Thiram 137-53-1, Dextrothyroxine sodium 137-58-6, Lidocaine 138-39-6, Mafenide 143-67-9, Vinblastine sulfate 143-71-5, Hydrocodone bitartrate 144-14-9, Anileridine 144-80-9, Sulfacetamide 144-82-1, Sulfamethizole 145-63-1, Suramin 146-22-5, Nitrazepam 146-54-3, Triflupromazine 147-85-3, Proline 147-94-4, Cytarabine 148-79-8, Thiabendazole 148-82-3, Melphalan 149-32-6, Erythritol 151-67-7,

Halothane 152-11-4, Verapamil hydrochloride 152-43-2, Quinestrol 152-47-6, Sulfalene 152-58-9, Cortodoxone 152-97-6, Fluocortolone 153-87-7, Oxypertine 154-21-2, Lincomycin 154-41-6, Phenylpropanolamine hydrochloride 154-42-7, Thioguanine 154-68-7, Antazoline phosphate 154-69-8, Tripelennamine hydrochloride 154-93-8, Carmustine 156-51-4, Phenelzine sulfate 271-95-4, 1,2-Benzisoxazole 297-76-7, Ethynodiol diacetate 298-46-4, Carbamazepine 298-57-7, Cinnarizine 298-59-9, Methylphenidate hydrochloride 299-39-8, Sparteine sulfate 299-42-3, Ephedrine 302-22-7, Chlormadinone acetate 302-49-8, Uredepa 302-79-4, Tretinoin 303-53-7, Cyclobenzaprine 304-20-1, Hydralazine hydrochloride 304-55-2, Succimer 304-84-7, Ethamivan 305-03-3, Chlorambucil 306-07-0, Pargyline hydrochloride 306-21-8, Hydroxyamphetamine hydrobromide 309-36-4, Methohexital sodium 314-19-2, Apomorphine hydrochloride 315-80-0, Dibenzepin hydrochloride 316-42-7, Emetine hydrochloride 317-52-2, Hexafluorenium bromide 318-98-9, Propranolol hydrochloride 319-89-1, Tetroquinone 320-67-2, Azacitidine 322-35-0, Benserazide 326-43-2, Phenyramidol hydrochloride 329-65-7, Racepinephrine 333-36-8, Flurothyl 338-98-7, Isoflupredone acetate 339-72-0, Levcycloserine 340-57-8, Mecloqualone 345-78-8, Pseudoephedrine hydrochloride 346-18-9, Polythiazide 356-12-7, Fluocinonide 357-07-3, Oxymorphone hydrochloride 357-70-0, Galantamine 359-83-1, Pentazocine 361-37-5, Methysergide 362-29-8, Propiomazine 363-20-2, Tricetamide 363-24-6, Dinoprostone 364-62-5, Metoclopramide 364-98-7, Diazoxide 366-70-1, Procarbazine hydrochloride 378-44-9, Betamethasone 379-79-3, Ergotamine tartrate 382-67-2, Desoximetasone 389-08-2, Nalidixic acid 390-64-7, Prenylamine 396-01-0, Triamterene 404-82-0, Fenfluramine hydrochloride 404-86-4, Capsaicin 406-90-6, Fluroxene 423-55-2, Perflubron 424-89-5, Clomegestone acetate 426-13-1, Fluorometholone 434-05-9, Methenolone acetate 434-07-1, Oxymetholone 435-97-2, Phenprocoumon 437-74-1, Xanthinol niacinate 439-14-5, Diazepam 440-17-5, Trifluoperazine hydrochloride 443-48-1, Metronidazole 446-86-6, Azathioprine 451-71-8, Glyhexamide 459-86-9, Mitoguazone 465-65-6, Naloxone 466-06-8, Proscillaridin 467-22-1, Carbiphene hydrochloride 472-15-1, Betulinic acid 474-25-9, Chenodiol 474-58-8, Sitogluside 474-86-2, Equilin 476-70-0, Boldine 480-30-8, Dichloralphenazone 480-39-7, Pinocembrin 483-63-6, Crotamiton 486-56-6, Cotinine 486-66-8, Daidzein 501-75-7
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release active ingredients)

IT 502-54-5, Monoctanoin 502-85-2, Sodium oxybate 503-49-1, Meglutol 504-24-5, Fampridine 506-26-3, Gamolenic acid 509-74-0, Methadyl acetate 511-13-7, Chlophedianol hydrochloride 513-10-0, Echothiophate iodide 514-36-3, Fludrocortisone acetate 514-65-8, Biperiden 517-09-9, Equilenin 518-28-5, Podofilox 520-85-4, Medroxyprogesterone 521-18-6, Dihydrotestosterone 522-48-5, Tetrahydrozoline hydrochloride 523-87-5, Dimenhydrinate 524-83-4, Ethybenztropine 525-26-8, Cloperidone hydrochloride 527-75-3, Berythromycin 528-43-8, Magnolol 528-53-0, Delphinidin 528-96-1, Benzoylpas calcium 530-08-5, Isoetharine 530-78-9, Flufenamic acid 532-03-6, Methocarbamol 533-45-9, Clomethiazole 536-33-4, Ethionamide 536-59-4, Perillyl alcohol 536-93-6, Eucatropine hydrochloride 538-23-8, Tricaprylin 541-15-1, Levocarnitine 541-79-7, Carbocloral 543-82-8, Octodrine 545-80-2, Poldine methylsulfate 547-81-9, 16-Epiestriol 548-04-9, Hypericin 548-57-2, Lucanthone hydrochloride 548-62-9, Gentian violet 548-68-5, Thiphenamil hydrochloride 549-18-8, Amitriptyline hydrochloride 550-70-9, Triprolidine hydrochloride 550-83-4, Propoxycaine hydrochloride 550-99-2, Naphazoline hydrochloride 551-11-1, Cyclosin 551-48-4, Guanoclor sulfate 552-94-3, Salsalate 554-57-4, Methazolamide 554-92-7, Trimethobenzamide hydrochloride 555-30-6, Methyldopa 555-43-1, Tristearin 555-44-2, Tripalmitin 555-65-7, Brocresine 555-84-0, Nifuradene 557-08-4, Zinc undecylenate 566-48-3, Formestane 569-57-3, Chlorotrianisene 578-95-0D, Acridone, imidazo derivs. 579-56-6, Isoxsuprine hydrochloride 581-88-4, Debrisoquin sulfate 585-86-4, Lactitol 587-61-1, Propyliodone 590-63-6, Bethanechol chloride 595-33-5, Megestrol acetate 596-51-0, Glycopyrrolate 599-79-1, Sulfasalazine 604-75-1, Oxazepam 606-05-3, Pyrabrom 609-78-9, Cycloguanil pamoate 614-39-1, Procainamide hydrochloride 630-56-8, Hydroxyprogesterone caproate 630-93-3,

Dilantin 631-06-1, Dexoxadrol hydrochloride 632-00-8, Sulfasomizole 632-99-5, Fuchsin 635-41-6, Trimetozine 636-54-4, Clopamide 637-07-0, Clofibrate 637-58-1, Pramoxine hydrochloride 638-23-3, Carbocysteine 638-94-8, Desonide 645-43-2, Guanethidine monosulfate 646-08-2, β-Alethine 651-06-9, Sulfameter 652-67-5, Isosorbide 653-03-2, Butaperazine 655-05-0, Thozalinone 655-35-6, Chromonar hydrochloride 657-24-9, Metformin 672-87-7, Metyrosine 679-90-3, Roflurane 692-13-7, Buformin 695-53-4, Dimethadione 720-76-3, Fluminorex 723-46-6, Sulfamethoxazole 729-99-7, Sulfamoxole 735-52-4, Cetophenicol 738-70-5, Trimethoprim 739-71-9, Trimipramine 742-20-1, Cyclopenthiazide 747-36-4, Hydroxychloroquine sulfate 749-02-0, Spiperone 749-13-3, Trifluperidol 751-94-0, Fusidate sodium 751-97-3, Rolitetracycline 773-76-2, Chloroxine 777-11-7, Haloprogin 797-63-7, Levonorgestrel 801-52-5, Porfiromycin 804-63-7, Quinine sulfate 808-26-4, Sancycline 811-97-2, Norflurane 826-39-1, Mecamylamine hydrochloride 829-74-3, Levonordefrin 846-49-1, Lorazepam 846-50-4, Temazepam 847-25-6, Racephenicol 848-75-9, Lormetazepam 852-19-7, Sulfazamet 852-42-6, Guaiapate 860-22-0 881-17-4 886-38-4, Diphencyprone 886-74-8, Chlorphenesin carbamate 894-71-3, Nortriptyline hydrochloride 896-71-9, Tigestol 909-14-8, Costatolide 909-39-7, Opipramol hydrochloride 911-45-5D, **Clomifene**, analogs 914-00-1, Methacycline 955-48-6, Metalol hydrochloride 956-90-1, Phencyclidine hydrochloride 959-10-4, Xenbucin 962-02-7, Nitrodan 963-39-3, Demoxepam 965-90-2, Ethylestrenol 967-48-6, Flubanilate hydrochloride 968-93-4, Testolactone 969-33-5, Cyproheptadine hydrochloride 972-02-1, Diphenidol 976-71-6, Canrenone 977-79-7, Medrogestone 980-71-2, Brompheniramine maleate 982-24-1, Clopenthixol 983-85-7, Penamecillin 985-16-0, Nafcillin sodium 987-02-0, Demecycline 987-78-0, Citicoline 990-73-8, Fentanyl citrate 1018-71-9, Pyrrolnitrin 1021-11-0, Guanoxyfen sulfate 1038-59-1, Glyoctamide 1050-48-2, Benzilonium bromide 1069-66-5, Valproate sodium 1070-11-7, Ethambutol hydrochloride 1070-95-7, Guanoctine hydrochloride 1094-08-2, Ethopropazine hydrochloride 1095-90-5, Methadone hydrochloride 1098-60-8, Triflupromazine hydrochloride 1104-22-9, Meclizine hydrochloride 1110-40-3, Cortivazol 1113-10-6, Guancydine 1115-70-4, Metformin hydrochloride 1134-47-0, Baclofen 1143-38-0, Anthralin 1146-98-1, Bromindione 1147-62-2, Pyrovalerone hydrochloride 1150-20-5, Azabon 1151-11-7, Ipodate calcium 1155-03-9, Zolamine hydrochloride 1156-19-0, Tolazamide 1172-18-5, Flurazepam hydrochloride 1173-88-2, Oxacillin sodium 1197-18-8, Cyclocapron 1197-21-3, Phentermine hydrochloride 1199-18-4, Oxidopamine 1211-28-5, Prolintane hydrochloride 1212-72-2, Mephentermine sulfate 1212-83-5, Guanisoquin sulfate 1218-35-5, Xylometazoline hydrochloride 1220-83-3, Sulfamonomethoxine 1225-20-3, Iothalamate sodium 1225-55-4, Protriptyline hydrochloride 1227-61-8, Mefexamide 1231-93-2, Ethynodiol 1232-85-5, Elantrine 1234-71-5, Namoxyrate 1235-15-0, Norbolethone 1242-56-4, Stenbolone acetate 1244-76-4 1252-69-3, Piperamide maleate 1253-28-7, Gestonorone caproate 1263-89-4, Paromomycin sulfate 1264-72-8, Colistin sulfate 1271-19-8, Titanocene dichloride 1314-95-0, Stannous sulfide 1319-82-0, Aminocaproic acid 1321-23-9, Chloroxylenol 1322-14-1, Calcium undecylenate 1323-83-7, Glycerol distearate 1336-78-3, Imidecyl iodine 1392-21-8, Kitasamycin 1397-89-3, Amphotericin B 1400-61-9, Nystatin 1402-82-0, Amphomycin 1403-17-4, Candicidin 1403-71-0, Hamycin 1403-99-2, Mitogillin 1404-00-8, Mitomycin 1404-08-6, Neutramycin 1404-15-5, Nogalamycin 1404-20-2, Peliomycin 1404-48-4, Relomycin 1404-59-7, Rutamycin 1404-64-4, Sparsomycin 1404-88-2, Tyrothricin 1404-90-6, Vancomycin 1404-93-9 1405-00-1, Viridofulvin 1405-20-5, Polymyxinbsulfate 1405-37-4, Capreomycin sulfate 1405-41-0, Gentamicin sulfate 1405-52-3, Sulfomyxin 1405-87-4, Bacitracin 1405-97-6, Gramicidin 1414-45-5, Nisin 1420-03-7, Propenzolate hydrochloride 1420-55-9, Thiethylperazine 1421-14-3, Propanidid 1424-00-6, Mesterolone 1432-75-3, Nitralamine hydrochloride 1456-52-6, Ioprocemic acid 1476-53-5, Novobiocin sodium 1477-40-3, Levomethadyl acetate 1491-81-2, Bolmantalate 1508-65-2, Oxybutynin chloride 1508-75-4, Tropicamide 1508-76-5, Procyclidine hydrochloride

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release active ingredients)

IT 1524-88-5, Flurandrenolide 1538-09-6 1553-34-0, Methixene hydrochloride 1553-60-2, Ibufenac 1597-82-6, Paramethasone acetate 1605-68-1, Taxane 1605-89-6, Bolasterone 1607-17-6, Pentrinitrol 1622-61-3, Clonazepam 1622-62-4, Flunitrazepam 1639-60-7, Propoxyphene hydrochloride 1642-54-2, Diethylcarbamazine citrate 1649-18-9, Azaperone 1661-29-6, Meturedepa 1665-48-1, Metaxalone 1684-40-8, Tacrine hydrochloride 1707-14-8, Phenmetrazine hydrochloride 1722-62-9, Mepivacaine hydrochloride 1740-22-3, Pyrinoline 1744-22-5, Riluzole 1764-85-8, Epithiazide 1786-81-8, Prilocaine hydrochloride 1808-12-4, Bromodiphenhydramine hydrochloride 1812-30-2, Bromazepam 1841-19-6, Fluspirilene 1847-63-8, Nafoxidine hydrochloride 1866-43-9, Rolodine 1867-66-9, Ketamine hydrochloride 1892-80-4, Fenethylline hydrochloride 1893-33-0, Pipamperone 1910-68-5, Methisazone 1977-10-2, Loxapine 1977-11-3, Perlapine 1980-45-6, Benzodepa 1982-37-2, Methdilazine 1986-53-4, Bolandiol dipropionate 2013-58-3, Meclocycline 2022-85-7, Flucytosine 2030-63-9, Clofazimine 2056-56-6, Cintazone 2058-52-8, Clothiapine 2062-78-4, Pimozide 2062-84-2, Benperidol 2068-78-2, Vincristine sulfate 2078-54-8, Propofol 2098-66-0, Cyproterone 2109-73-1, Butacetin 2119-75-7, Fluperolone acetate 2127-01-7, Clorexolone 2135-14-0, Descinolone acetonide 2135-17-3, Flumethasone 2152-34-3, Pemoline 2154-02-1, Methopholine 2167-85-3, Pipazethate 2169-64-4, Azaribine 2181-04-6, Canrenoate potassium 2210-77-7, Pyrrocaine 2218-68-0, Chloral betaine 2244-21-5, Troclosene potassium 2259-96-3, Cyclothiazide 2276-90-6, Iothalamic acid 2313-87-3, Ethoxazene hydrochloride 2315-02-8, Oxymetazoline hydrochloride 2321-07-5, Fluorescein 2324-94-9, Profadol hydrochloride 2353-33-5, Decitabine 2364-72-9, Cyprolidol hydrochloride 2391-03-9, Dexbrompheniramine maleate 2398-96-1, Tolnaftate 2438-32-6, Dexchlorpheniramine maleate 2441-88-5, Fenyripol hydrochloride 2447-57-6, Sulfadoxine 2465-59-0, Oxypurinol 2487-63-0, Quinbolone 2508-79-4, Methyldopate hydrochloride 2521-01-9, Encyprate 2529-45-5, Flurogestone acetate 2607-06-9, Diflucortolone 2608-24-4, Piposulfan 2612-33-1, Clonitrate 2618-25-9, Ioglycamic acid 2668-66-8, Medrysone 2687-96-9 2740-04-7, Dimefline hydrochloride 2750-76-7, Rifamide 2751-09-9, Troleandomycin 2753-45-9, Mebeverine hydrochloride 2768-90-3, Quinaldine blue 2809-21-4, Etidronic acid 2825-60-7, Formocortal 2829-19-8, Rolicyprine 2856-75-9, Modaline sulfate 2898-11-5, Medazepam hydrochloride 2898-13-7, Sulazepam 2919-66-6, Melengestrol acetate 2921-92-8, Propatyl nitrate 2955-38-6, Prazepam 2975-34-0, Carphenazine maleate 2988-32-1, Indriline hydrochloride 2998-57-4, Estramustine 3000-39-3, Quingestanol acetate 3044-32-4, Clogestone acetate 3056-17-5, Stavudine 3073-59-4, Hexamethylene bisacetamide 3093-35-4, Halcinonide 3105-97-3, Hycanthone 3115-05-7, Iobenzamic acid 3116-76-5, Dicloxacillin 3122-01-8, Thiazesim hydrochloride 3124-93-4, Ethynerone 3137-73-3, Anagestone acetate 3200-06-4, Nafronyl oxalate 3202-55-9, Benapryzine hydrochloride 3211-76-5, Selenomethionine 3239-45-0, Dexfenfluramine hydrochloride 3270-71-1, Nifuraldezone 3282-75-5, Ethanolamine oleate 3313-26-6, Thiothixene 3374-05-8, Nalidixate sodium 3385-03-3, Flunisolide 3416-26-0, Lidoflazine 3440-28-6, Betamipron 3459-20-9, Glymidine sodium 3485-14-1, Cyclacillin 3485-62-9, Clidinium bromide 3505-38-2, Carbinoxamine maleate 3511-16-8, Hetacillin 3521-84-4, Iodipamide meglumine 3538-57-6, Haloprogesterone 3546-41-6, Pyrvinium pamoate 3562-84-3, Benzbromarone 3570-10-3, Benorterone 3570-75-0, Nifurthiazole 3572-80-3, Cyclazocine 3577-01-3, Cephaloglycin 3599-32-4, Indocyanine green 3601-19-2, Ropizine 3614-69-5, Dimethindene maleate 3624-96-2, Bialamicol hydrochloride 3666-69-1, Dioxadrol hydrochloride 3688-85-5, Diapamide 3693-39-8, Flucloronide 3696-28-4, Dipyrithione 3704-09-4, Mibolerone 3715-90-0, Tramazoline hydrochloride 3717-88-2, Flavoxate hydrochloride 3734-16-5, Prodilidine hydrochloride 3735-90-8, Phencarbamide 3737-09-5, Disopyramide 3771-19-5, Nafenopin 3778-73-2, Ifosfamide 3784-99-4, Stilbazium iodide 3791-63-7 3795-88-8, Levofuraltadone 3810-74-0, Streptomycin sulfate 3810-80-8, Diphenoxylate hydrochloride 3819-00-9, Piperacetazine 3845-22-5, Teroxalene hydrochloride 3858-89-7, Chloroprocaine hydrochloride 3861-73-2, Anazolene sodium 3876-10-6, Clominorex 3930-19-6, Streptonigrin 3930-20-9, Sotalol 3978-86-7, Azatadine maleate 4015-32-1, Quazodine 4105-38-8 4117-65-1, Aspartocin 4171-13-5, Valnoctamide 4197-24-4, Carbol-Fuchsin

4205-90-7, Clonidine 4258-85-9, Clocortolone acetate 4268-36-4, Tybamate 4291-63-8, Cladribine 4320-13-2, Thiazinamium chloride 4330-99-8, Trimeprazine tartrate 4342-03-4, Dacarbazine 4386-35-0, Meralein sodium 4434-20-2, Clothixamide maleate 4499-40-5, Oxtriphylline 4548-15-6, Flunidazole 4551-59-1, Fenalamide 4598-67-8 4663-83-6, Buramate 4682-36-4, Orphenadrine citrate 4724-59-8, Clamoxyquin hydrochloride 4759-48-2, Isotretinoin 4803-27-4, Anthramycin 4803-44-5, Levopropylcillin potassium 4803-45-6, Thiphencillin potassium 4936-47-4, Nifuratel 4991-68-8, Pimetine hydrochloride 5002-47-1, Fluphenazine decanoate 5034-76-4, Indoxole 5036-03-3, Nifurdazil 5051-62-7, Guanabenz 5053-06-5, Fenspiride 5055-20-9, Nifurquinazol 5055-42-5, Silandrone 5072-26-4, Buthionine sulfoximine 5086-74-8, Tetramisole hydrochloride 5090-37-9, Metizoline hydrochloride 5104-49-4, Flurbiprofen 5118-17-2, Furazolium chloride 5250-39-5, Floxacillin 5251-34-3, Cloprednol 5289-74-7, Ecdysterone 5318-76-3, Imidocarb hydrochloride 5322-53-2, Oxiperomide 5355-16-8, Diaveridine 5370-01-4, Mexiletine hydrochloride 5373-42-2, Thaliblastine 5467-78-7, Fenamole 5490-27-7, Dihydrostreptomycin sulfate 5508-58-7, Andrographolide 5522-33-8, Difluanine hydrochloride 5534-09-8, Beclomethasone dipropionate 5536-17-4, Vidarabine 5560-62-3, Biphenamine hydrochloride 5560-69-0, Ethyl dibunate 5560-72-5, Iprindole 5560-73-6, Mimbane hydrochloride 5560-75-8, Pyroxamine maleate 5560-77-0, Rotoxamine 5560-78-1, Teclozan 5578-73-4, Sanguinarium chloride 5579-13-5, Capuride 5579-16-8, Epinephryl borate 5579-27-1, Simtrazene 5579-85-1, Bromchlorenone 5579-92-0, Iopydol 5579-93-1, Iopydone 5579-94-2, merisoprol Hg 197 5579-95-3, Nifurmerone 5581-35-1, Amphecloral 5581-40-8, Dimefadane 5581-42-0, Glyparamide 5581-46-4, Molinazone
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release active ingredients)

IT 5581-52-2, Thiamiprine 5585-59-1, Nitrocycline 5585-60-4, Paranyline hydrochloride 5585-62-6 5585-71-7, Benzindopyrine hydrochloride 5585-73-9, Butriptyline hydrochloride 5586-87-8, Mefenorex hydrochloride 5588-20-5, Chlordantoin 5588-21-6, Cintriamide 5588-23-8, Cypenamine hydrochloride 5588-25-0, Dihexyverine hydrochloride 5588-29-4, Fenmetramide 5588-31-8, Imidoline hydrochloride 5588-33-0, Mesoridazine 5588-38-5, Tolpyrramide 5591-22-0, Becanthone hydrochloride 5591-27-5, Clometherone 5591-29-7, Etafedrine hydrochloride 5591-33-3, Iosefamic acid 5591-43-5, Solypertine tartrate 5591-44-6, Pyrroliphene hydrochloride 5611-64-3, Methalthiazide 5630-53-5, Tibolone 5633-14-7, Benzetimide hydrochloride 5633-25-0, Noracymethadol hydrochloride 5634-37-7, Clorethate 5634-38-8, Guaithylline 5634-40-2, Levamfetamine succinate 5634-41-3, Parapenzolate bromide 5634-42-4, Tocamphyl 5667-70-9, Pentabamate 5667-71-0, Streptonicozid 5696-06-0, Methetoin 5696-09-3, Proxazole 5696-15-1, Butoxamine hydrochloride 5696-17-3, Epipropidine 5714-04-5, Guanoxan sulfate 5714-05-6, Quindecamine acetate 5714-75-0, Prednazate 5714-76-1, Quinetolate 5714-82-9, Triclofenol piperazine 5714-90-9, Levopropoxyphene napsylate 5716-20-1, Bamethan sulfate 5728-52-9, Felbinac 5749-67-7, Carbaspirin calcium 5781-37-3, Cycliramine maleate 5786-21-0, Clozapine 5786-68-5, Quipazine maleate 5800-19-1, Metiapine 5863-35-4, Nitromifene citrate 5870-29-1, Cyclopentolate hydrochloride 5875-06-9, Proparacaine hydrochloride 5928-84-7, Penicillinvbenzathine 5964-24-9, Thimerfonate sodium 5965-13-9, Dihydrocodeine bitartrate 5977-10-6, Fencibutirol 5980-31-4, Hexedine 5987-82-6, Benoxinate hydrochloride 6054-98-4, Olsalazine sodium 6157-87-5, Trestolone acetate 6190-39-2, Dihydroergotamine mesylate 6284-40-8, Meglumine 6385-02-0, Meclofenamate sodium 6385-58-6, Bithionolate sodium 6443-40-9, Xylamidine tosylate 6452-73-9, Oxprenolol hydrochloride 6493-05-6, Pentoxifylline 6500-81-8, Ethacrynate sodium 6533-00-2, Norgestrel 6556-11-2, Inositol niacinate 6576-51-8, Stallimycin hydrochloride 6591-72-6, Penicillinvhydrabamine 6620-60-6, Proglumide 6639-99-2, 17-α-Dihydroequilenin 6673-35-4, Practolol 6673-97-8, Spiroxasone 6724-53-4, Perhexiline maleate 6804-07-5, Carbadox 6830-17-7, Oxamarin hydrochloride 6890-40-0, Histamine phosphate 6933-90-0, Clorprenaline hydrochloride 6981-18-6, Ormetoprim 6990-06-3, Fusidic acid 7004-98-0, Epimestrol 7013-41-4, Talopram

hydrochloride 7019-69-4 7054-25-3, Quinidine gluconate 7082-27-1, Trimoxamine hydrochloride 7082-29-3, Ampyzine sulfate 7082-30-6, Triampyzine sulfate 7125-67-9, Metoquizine 7125-70-4, Amiquinsin hydrochloride 7125-71-5, Toquizine 7125-73-7, Flumetramide 7125-76-0, Codoxime 7195-27-9, Mefruside 7199-29-3, Cyheptamide 7225-61-8, Metrizoate sodium 7232-51-1, Pararosaniline pamoate 7241-94-3, Zolertine hydrochloride 7246-20-0, Triclofos sodium 7246-21-1, Tyropanoate sodium 7247-57-6, Heteronium bromide 7261-97-4, Dantrolene 7262-00-2, Quinazosin hydrochloride 7273-99-6, Gamfexine 7280-37-7, Estropipate 7281-31-4, Vinglycinate sulfate 7297-25-8, Erythrityl tetranitrate 7414-83-7, Etidronate disodium 7421-40-1, Carbenoxolone sodium 7424-00-2, Fenclonine 7439-94-3, Lutetium 7439-97-6, Mercury 7440-06-4D, Platinum, compds. 7440-57-5, Gold 7447-40-7, Potassium chloride 7481-89-2, Zalcitabine 7487-88-9, Magnesium sulfate 7491-74-9, Piracetam 7492-29-7, Clazolam 7553-56-2, Iodine 7554-65-6, Fomepizole 7601-55-0, Metocurine iodide 7644-67-9, Azotomycin 7660-71-1, Mesuprine hydrochloride 7681-11-0, Potassium iodide 7681-54-1, Indomethacin sodium 7681-76-7, Ronidazole 7681-80-3, Pentapiperium methylsulfate 7681-93-8, Natamycin 7689-03-4D, Camptothecin, derivs. 7698-97-7, Fenestrel 7720-78-7, Ferrous sulfate 7722-64-7, Potassium permanganate 7722-84-1, :Hydrogen peroxide 7724-76-7, Riboprine 7761-45-7, Metoprine 7761-88-8, Silver nitrate 8008-53-5, Ethiodized Oil 8017-57-0, Trisulfapyrimidine 8025-81-8, Spiramycin 8029-68-3, Ichthammol 8029-99-0, Paregoric 8031-09-2, Sodium morrhuate 8031-14-9, Oxychlorosene 8052-16-2, Cactinomycin 8063-91-0, Mirincamycin hydrochloride 8065-29-0, Liotrix 8067-24-1, Ergoloid mesylates 8067-69-4, Halquinols 8068-28-8, Colistimethate sodium 9000-99-1, Brinolase 9002-04-4, Thrombin 9002-60-2, Corticotropin 9002-61-3, Human chorionic gonadotropin 9002-67-9, Luteinizing hormone 9002-69-1, Relaxin 9003-20-7, Polyvinyl acetate 9003-21-8, Poly (methyl acrylate) 9003-42-3, Poly(ethyl methacrylate) 9003-63-8, Poly(butyl methacrylate) 9004-10-8, Insulin 9004-35-7 9004-36-8, Cellulose acetate butyrate 9004-38-0, Cellulose acetate phthalate 9004-39-1, Cellulose acetate propionate 9004-48-2, Cellulose propionate 9004-57-3, Ethylcellulose 9007-12-9, Calcitonin 9007-92-5, Glucagon 9008-05-3, Histoplasmin 9010-01-9, Sodium amylosulfate 9010-88-2, eudragit NE30D 9011-14-7, Poly(methyl methacrylate) 9011-15-8, Poly(isobutyl methacrylate) 9011-93-2, Lysostaphin 9012-09-3 9012-76-4, Poliglusam 9014-02-2, Zinostatin 9014-42-0, Thrombopoietin 9015-68-3, Asparaginase 9039-53-6, Urokinase 9041-08-1, Ardeparin sodium 9041-93-4, Bleomycin sulfate 9046-56-4, Ancrod 9050-67-3, Sizofiran 9051-97-2D, 1,3-β-Glucan, carboxymethylated 9054-89-1, Orgotein 9087-70-1, Aprotinin 10024-97-2, Nitrous oxide 10043-49-9, Au 198 10078-46-3, Roletamide 10085-81-1, Benzoctamine hydrochloride 10087-89-5, Enpromate 10118-85-1, Lydimycin 10118-90-8, Minocycline 10238-21-8, Glyburide 10262-69-8, Maprotiline 10310-32-4, Tribenoside 10318-26-0, Mitolactol 10322-73-3, Estrofurate 10351-50-5, Leniquinsin 10355-14-3, Boxidine 10389-72-7, Clortermine hydrochloride 10397-75-8, Iocarmic acid 10403-51-7, Mitindomide 10418-03-8, Stanozolol 10423-37-7, Citenamide 10457-90-6, Bromperidol 10488-36-5 10540-29-1, Tamoxifen 10540-97-3, Memotine hydrochloride 10549-91-4, Meclorisone dibutyrate 10563-70-9, Melitracen hydrochloride 10596-23-3, Clodronic acid 11000-17-2, Vasopressin 11002-22-5, Apurinic acid 11006-76-1, Virginiamycin 11006-77-2, Statolon 11015-37-5, Bambermycin 11016-07-2, Fungimycin 11028-00-5, Bacoside A 11029-06-4, Elemene 11033-34-4, Steffimycin 11041-12-6, Cholestyramine resin 11043-98-4, Mitocromin 11043-99-5, Mitomalcin 11048-13-8, Nebramycin 11048-15-0, Kalafungin 11048-52-5 11051-71-1, Avilamycin 11056-09-0, Ranimycin 11056-11-4, Biniramycin 11056-12-5, Cirolemycin 11056-13-6, Denofungin 11056-14-7, Mitocarcin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release active ingredients)

IT 11056-15-8, Mitosper 11056-18-1, Scopafungin 11056-20-5, Zorbamycin 11078-21-0, Filipin 11096-49-4, Partricin 11121-32-7, Mepartricin 12192-57-3, Aurothioglucose 12622-73-0, Coccidioidin 12629-01-5, Somatropin 12706-94-4, Anthelmycin 12713-07-4D, Verdin, derivs. 13010-47-4, Lomustine 13055-82-8, Reproterol hydrochloride 13060-14-5, Yangambin 13071-11-9, Dexpropranolol hydrochloride 13103-34-9,

Boldenone undecylenate 13115-40-7, Fonazine mesylate 13292-46-1, Rifampin 13379-87-8, Tiprenolol hydrochloride 13392-18-2, Fenoterol 13392-28-4, Rimantadine 13408-29-2, Nitroxide 13411-16-0, Nifurpirinol 13422-16-7, Triflocin 13463-41-7, Pyrithione zinc 13494-90-1, Gallium nitrate 13523-86-9, Pindolol 13539-59-8, Apazone 13551-87-6, Misonidazole 13647-35-3, Trilostane 13665-88-8, Mopidamol 13698-49-2, Delmadinone acetate 13758-23-1, Quinterenol sulfate 13838-16-9, Enflurane 13909-09-6, Semustine 13958-40-2, Oxiramide 14008-44-7, Metopimazine 14008-46-9, Pinoxepin hydrochloride 14028-44-5, Amoxapine 14088-71-2, Proclonol 14176-10-4, Cetiedil 14176-50-2, Tiletamine hydrochloride 14188-82-0, Cytostatin 14255-87-9, Parbendazole 14265-71-5, selenium 75 14293-44-8, Xipamide 14402-89-2, Sodium nitroprusside 14437-41-3, Clioxanide 14484-47-0, Deflazacort 14561-42-3, Menoctone 14611-51-9, Selegiline 14611-52-0, Selegiline hydrochloride 14636-12-5, Terlipressin 14698-29-4, Oxolinic acid 14769-73-4, Levamisole 14769-74-5, Dexamisole 14796-24-8, Cinperene 14796-28-2, Clodanolene 14816-67-2, Soterenol hydrochloride 14885-29-1, Ipronidazole 14930-96-2, Cytochalasin B 15037-55-5, Ethonam nitrate 15176-29-1, Edoxudine 15179-97-2, Estrazinol hydrobromide 15180-00-4, Prednival 15221-81-5, Fludorex 15256-58-3, Beloxamide 15307-79-6, Diclofenac sodium 15318-45-3, Thiamphenicol 15468-10-7, Oxidronic acid 15478-78-1, Iodamide 15500-66-0, Pancuronium bromide 15574-96-6, Pizotyline 15578-26-4, Stannous pyrophosphate 15622-65-8, Molindone hydrochloride 15639-50-6, Safingol 15663-27-1, Cisplatin 15676-16-1, Sulpiride 15686-51-8, Clemastine 15686-68-7, Volazocine 15686-71-2, Cephalexin 15686-74-5, Cyclophenazine hydrochloride 15686-91-6, Propiram 15687-07-7, Cyprazepam 15687-27-1, Ibuprofen 15722-48-2, Olsalazine 15793-40-5, Terodiline 15826-37-6, Cromolyn sodium 15922-78-8, Pyrithione sodium 15992-13-9, Intrazole 16034-77-8, Iocetamic acid 16051-77-7, Isosorbide mononitrate 16231-75-7, Atolide 16320-04-0, Gestrinone 16590-41-3, Naltrexone 16624-40-1 16662-47-8, Gallopamil 16676-27-0, Nalmexone hydrochloride 16679-58-6, Desmopressin 16773-42-5, Ornidazole 16816-67-4, Pantethine 16846-24-5, Josamycin 16915-71-2, Cingestol 16915-78-9, Bolenol 16915-79-0, Mequidox 16915-80-3, Oxogestone phenpropionate 16960-16-0, Cosyntropin 17021-26-0, Calusterone 17033-82-8, iomethini125 17090-79-8, Monensin 17196-88-2, Vincofos 17230-85-2, Amquinate 17230-86-3, Carbenicillin potassium 17230-87-4, Seperidol hydrochloride 17230-88-5, Danazol 17230-89-6, Nimazone 17243-32-2, Ketipramine fumarate 17243-64-0, Piprozolin 17289-49-5, Tetrydamine 17321-77-6, Clomipramine hydrochloride 17560-51-9, Metolazone 17598-65-1, Deslanoside 17605-73-1, Colterol mesylate 17650-98-5, Ceruletide 17737-65-4, Clonixin 17784-12-2, Sulfacytine 17902-23-7, Tegafur 18010-40-7, Bupivacaine hydrochloride 18046-21-4, Fentiazac 18109-81-4, Butamirate citrate 18174-58-8, Pipoxolan hydrochloride 18323-44-9, Clindamycin 18378-89-7, Plicamycin 18416-85-8, Lombricine 18464-39-6, Caroxazone 18472-51-0, Chlorhexidine gluconate 18559-94-9, Salbutamol 18588-57-3, Etoprine 18641-57-1, Glyceryl behenate 18694-40-1, Epirizole 18883-66-4, Streptozocin 18917-89-0, Magnesium salicylate 18965-97-4, Berlafenone 18984-80-0, Euprocin hydrochloride 19216-56-9, Prazosin 19237-84-4, Prazosin hydrochloride 19291-69-1, Gestaclone 19356-17-3, Calcifediol 19561-70-7, Nifuratrone 19825-63-9, Pirnabine 19863-06-0, Ioxotrizoic acid 19885-51-9, Aranotin 19888-56-3, Fluazacort 19916-73-5, O6-Benzylguanine 19992-80-4, Butixirate 20064-19-1, Propionylcarnitine 20098-14-0, Idramantone 20187-55-7, Bendazac 20287-37-0, Fenquizone 20350-15-6, Brefeldin 20423-99-8, Deprodone 20554-84-1, Parthenolide 20559-55-1, Oxibendazole 20638-84-0, Retinamide 20684-06-4, Bamifylline hydrochloride 20830-75-5, Digoxin 21059-48-3, Veramine 21132-59-2, Pazoxide 21221-18-1, Flazalone 21256-18-8, Oxaprozin 21365-49-1, Tralonide 21434-91-3, Capobenic acid 21440-97-1, Brofoxine 21498-08-8, Lofexidine hydrochloride 21535-47-7, Mianserin hydrochloride 21626-89-1, Diftalone 21638-36-8, Nifurimide 21736-83-4, Spectinomycin hydrochloride 21738-42-1, Oxamniquine 21791-39-9, Letimide hydrochloride 21820-82-6, Fenpipalone 21829-22-1, Clonixeril 21829-25-4, Nifedipine 21888-98-2, Dexetimide 21925-88-2, Tesicam 22012-72-2, Zilantel 22071-15-4, Ketoprofen 22161-81-5, Dexketoprofen 22195-34-2, Guanadrel sulfate 22199-46-8, Clomacran phosphate

22204-24-6, Pyrantel Pamoate 22204-53-1, Naproxen 22204-91-7, Lifibrate 22232-71-9, Mazindol 22254-24-6, Ipratropium bromide 22316-47-8, Clobazam 22365-40-8, Triflubazam 22461-13-8, Fantridone hydrochloride 22484-64-6, Sulfanilate zinc 22494-27-5, Flufenisal 22494-42-4, Diflunisal 22632-06-0, Bupicomide 22662-39-1, Rafoxanide 22664-55-7, Metipranolol 22668-01-5, Etanidazole 22737-01-5, Diflumidone sodium 22760-18-5, Proquazone 22916-38-7, Orconazole nitrate 22916-47-8, Miconazole 23031-32-5, Terbutaline sulfate 23076-35-9, Xylazine hydrochloride 23092-17-3, Halazepam 23155-02-4, Fosfomycin 23163-51-1, Methynodiol diacetate 23226-37-1, Daledalin tosylate 23239-36-3, Deterenol hydrochloride 23239-37-4, Etoxadrol hydrochloride 23239-41-0, Cephacetrile sodium 23239-78-3, Pridefine hydrochloride 23247-36-1, Nafomine malate 23256-09-9, Closiramine aceturate 23256-26-0, Piquizil hydrochloride 23256-28-2, Hoquizil hydrochloride 23256-50-0, Guanabenz acetate 23257-58-1, Levoxadrol hydrochloride 23277-43-2, Nalbuphine hydrochloride 23277-50-1, Salicylate meglumine 23288-49-5, Probucol 23313-80-6, Epitetracycline hydrochloride 23319-48-4, Megalomicin potassium phosphate 23327-57-3, Nefopam hydrochloride 23444-86-2, Suncillin sodium 23469-05-8, Diamocaine cyclamate 23478-02-6, 16-α-Gitoxin 23486-22-8, Esproquin hydrochloride 23541-50-6, Daunorubicin hydrochloride 23593-75-1, Clotrimazole
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release active ingredients)

IT 23607-71-8, Fetoxylate hydrochloride 23672-07-3, Levosulpiride 23674-86-4, Difluprednate 23712-05-2, Fenmetozole hydrochloride 23736-58-5, Cloxacillin benzathine 23757-42-8, Midaflur 23779-99-9, Floctafenine 23915-74-4, Trebenzomine hydrochloride 24047-25-4, Guanoxabenz 24233-80-5, Bisobrin lactate 24243-89-8, Triflumidate 24280-93-1, Mycophenolic acid 24305-27-9, Protirelin 24353-88-6, Lorbamate 24356-60-3, Cephapirin sodium 24357-98-0, Isomylamine hydrochloride 24358-76-7, Nivazol 24358-84-7, Dexivacaine 24359-14-6, liothyroninei125 24359-16-8 24360-55-2, Milipertine 24381-55-3, Salethamide maleate 24428-71-5, Glicetanile sodium 24584-09-6, Dexrazoxane 24678-13-5, Lenperone 24967-94-0, Dermatan sulfate 25053-27-4, Lyapolate sodium 25087-17-6, Poly (hexyl methacrylate) 25092-41-5, Norgestomet 25122-46-7, Clobetasol propionate 25122-57-0, Clobetasone butyrate 25126-32-3, Sincalide 25127-31-5, Cidoxepin hydrochloride 25155-18-4, Methylbenzethonium chloride 25189-01-9, Poly(phenyl methacrylate) 25269-04-9, Nisobamate 25314-87-8, Elucaine 25332-39-2, Trazodone hydrochloride 25387-70-6, Dazadrol maleate 25389-94-0, Kanamycin sulfate 25451-15-4, Felbamate 25496-72-4, Glycerol monooleate 25614-03-3, Bromocriptine 25655-41-8, Povidone-Iodine 25717-80-0, Molsidomine 25719-52-2, Poly (lauryl methacrylate) 25775-90-0, Zucapsaicin 25812-30-0, Gemfibrozil 25827-13-8, Suloxifen oxalate 25905-77-5, Minaprine 25953-19-9, Cefazolin 25986-77-0, Poly (octadecyl acrylate) 26048-05-5, Beauvericin 26097-80-3, Cambendazole 26124-32-3, Poly (isopropyl acrylate) 26155-31-7, Morantel tartrate 26159-36-4, Naproxol 26171-23-3, Tolmetin 26304-61-0, Azepindole 26308-28-1, Ripazepam 26309-95-5, Pivampicillin hydrochloride 26335-74-0, Poly (isobutyl acrylate) 26538-44-3, Zeranol 26615-21-4, Zotepine 26652-09-5, Ritodrine 26675-46-7, Isoflurane 26718-25-2, Halofenate 26774-90-3, Epicillin 26786-32-3, Lofepramine hydrochloride 26786-84-5, Lomofungin 26787-78-0, Amoxicillin 26807-65-8, Indapamide 26839-75-8, Timolol 26844-12-2, Indoramin 26849-57-0, Triclonide 26864-56-2, Penfluridol 26944-48-9, Glibornuride 27107-79-5, Tilidine hydrochloride 27220-47-9, Econazole 27223-35-4, Ketazolam 27262-47-1, Levobupivacaine 27276-25-1, Capobenate sodium 27302-90-5, Oxisuran 27314-97-2, Tirapazamine 27466-29-1, Intriptyline hydrochloride 27511-99-5, Eterobarb 27523-40-6, Isoconazole 27548-93-2, baccatin III 27589-33-9, Azosemide 27591-69-1, Tilorone hydrochloride 27686-84-6, Masoprocol 27724-96-5, Cetraxate hydrochloride 27737-38-8, Mixidine 27762-78-3, Kethoxal 27823-62-7, Chlortetracycline bisulfate 27848-84-6, Nicergoline 27877-51-6, Tolindate 28069-65-0, Cuprimyxin 28395-03-1 28523-86-6, Sevoflurane 28546-58-9, Uldazepam 28657-80-9, Cinoxacin 28721-07-5, Oxcarbazepine 28745-68-8, Thiofedrine 28782-42-5, Difenoxin 28841-62-5, Atrinositol 28860-95-9, Carbidopa

28911-01-5, Triazolam 29050-11-1, Seclazone 29053-27-8, Meseclazone
29069-24-7, Prednimustine 29094-61-9, Glipizide 29110-48-3, Guanfacine
hydrochloride 29121-60-6, Vaninolol 29122-68-7, Atenolol 29334-07-4,
Sulmarin 29342-05-0, Ciclopirox 29462-18-8, Bentazepam 29679-58-1,
Fenoprofen 29767-20-2, Teniposide 29868-97-1, Pirenzepine
hydrochloride 29975-16-4, Estazolam 30060-91-4, Lometraline
hydrochloride 30236-32-9, Dexsotalol 30303-65-2, Docosanol
30387-51-0, Asperlin 30392-41-7, Bitolterol mesylate 30516-87-1,
Zidovudine 30544-47-9, Etofenamate 30652-11-0, Deferiprone
30716-01-9, Emilium tosylate 30868-30-5, Pyrazofurin 30910-27-1,
Treloxinate 31112-62-6, Metrizamide 31127-82-9, Iodoxamide
31428-61-2, Tiamenidine 31430-15-6, Flubendazole 31430-18-9,
Nocodazole 31431-39-7, Mebendazole 31431-43-3, Cyclobendazole
31441-78-8, Mercaptopurine 31478-45-2, Bamnidazole 31677-93-7,
Bupropion hydrochloride 31793-07-4, Pirprofen 31842-01-0, Indoprofen
31842-61-2, Rimiterol hydrobromide 31855-75-1 31883-05-3, Moracizine
31932-09-9, Ticarbodine 31959-88-3, Clodazon hydrochloride 31969-05-8,
Bunolol hydrochloride 32211-97-5, Cyclindole 32222-06-3, Calcitriol
32266-10-7, Hexoprenaline sulfate 32295-18-4, Tosifen 32385-11-8,
Sisomicin 32462-30-9, Oxfenicine 32780-64-6, Labetalol hydrochloride
32795-47-4, Nomifensine maleate 32954-58-8, Ipomeanol 32986-56-4,
Tobramycin 33025-33-1 33069-62-4, Paclitaxel 33089-61-1, Amitraz
33125-97-2, Etomidate 33144-79-5, Broperamole 33159-27-2, Ecabet
33237-74-0, Aprindine hydrochloride 33286-22-5, Diltiazem hydrochloride
33386-08-2, Buspirone hydrochloride 33402-03-8, Metaraminol bitartrate
33419-42-0, Etoposide 33434-24-1, eudragit RL 33515-09-2, Gonadorelin
33564-31-7, Diflorasone diacetate 33754-49-3, Zolazepam hydrochloride
33765-68-3, Oxendolone 33774-52-6, Detajmium bitartrate 33813-84-2,
Deprostil 33876-97-0, Linsidomine 34031-32-8, Auranofin 34042-85-8,
Sudoxicam 34061-34-2 34114-01-7, Pemerid nitrate 34144-82-6
34157-83-0, Celastrol 34183-22-7, Propafenone hydrochloride
34214-49-8, Phenbutazone sodium glycerate 34256-91-2, Naranol
hydrochloride 34297-34-2, Anidoxime 34368-04-2, Dobutamine
34444-01-4, Cefamandole 34482-99-0, Fletazepam 34522-46-8, Oxetorone
fumarate 34552-83-5, Loperamide hydrochloride 34552-84-6, Isoxicam
34580-14-8, Ketotifen fumarate 34645-84-6, Fenclofenac 34661-75-1,
Urapidil 34839-70-8, Metiamide 34866-46-1, Carbuterol hydrochloride
34887-52-0, Fenisorex 34966-41-1, Cartazolate 35100-44-8, Endrysone
35115-60-7, Teprotide 35121-78-9, Epoprostenol 35135-67-2,
Cormethasone acetate 35189-28-7, Norgestimate 35212-22-7, Ipriflavone
35273-88-2, Gliflumide 35301-24-7, Cedefingol 35322-07-7, Fosazepam
35423-09-7, Tesimide 35425-83-3, Quinuclium bromide 35449-36-6,
Gemcadiol 35523-45-6, Fludalanine 35554-44-0, Enilconazole
35578-20-2, Oxarbazole 35604-67-2, Viloxazine hydrochloride
35607-20-6, Avridine 35607-66-0, Cefoxitin 35700-23-3, Carboprost
35764-29-5, Fluotracen hydrochloride 35795-17-6, Trimazosin
hydrochloride 35834-26-5, Rosaramicin 35838-58-5, Etazolate
hydrochloride 35846-53-8, Maitansine 35941-71-0, Tiaramide
hydrochloride 35943-35-2, Triciribine 36167-63-2, Halofantrine
hydrochloride 36282-47-0, Tramadol hydrochloride 36292-69-0,
Ketazocine 36322-90-4, Piroxicam 36330-85-5, Fenbufen 36504-94-6,
Butaclamol hydrochloride 36505-82-5, Prodolic acid 36508-71-1,
Zorubicin hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release
active ingredients)

IT 36616-52-1, Fenclorac 36637-18-0, Etidocaine 36653-82-4, Cetyl alcohol
36735-22-5, Quazepam 36740-73-5, Flumizole 36791-04-5, Ribavirin
36945-03-6, Lergotrile 36950-96-6, Cicloprofen 36981-91-6, Fepradinol
36983-81-0, Fosfonet sodium 37025-55-1, Carbetocin 37087-94-8, Tibric
acid 37091-66-0, Azlocillin 37106-97-1, Bentiromide 37200-12-7,
Poly(isodecyl methacrylate) 37270-89-6, Nadroparin calcium 37296-80-3
37321-09-8, Apramycin 37332-99-3, Avoparcin 37517-26-3, Pipotiazine
palmitate 37554-40-8, Fluquazone 37640-71-4, Aprindine 37661-08-8,
Bacampicillin hydrochloride 37686-84-3, Terguride 37717-21-8,
Flurocitabine 37723-78-7, Iopronic acid 37750-83-7, Rimoprogin
37751-39-6, Ciclazindol 37800-79-6 37863-70-0, Iosumetic acid
38070-41-6, Tiodonium chloride 38081-67-3, Carmantadine 38103-61-6,
Tolamolol 38194-50-2, Sulindac 38241-28-0, Zinterol hydrochloride

38241-39-3, Tazolol hydrochloride 38270-90-5, strontium chloride Sr 89 38274-54-3, Benurestat 38304-91-5, Minoxidil 38321-02-7, Dexverapamil 38363-32-5, Penbutolol sulfate 38677-85-9, Flunixin 38821-53-3, Cephradine 38821-80-6, Rodocaine 38873-55-1, Furobufen 38955-22-5, Pinadoline 39022-39-4, Oxaprotiline hydrochloride 39186-49-7, Pirolazamide 39236-46-9, Imidurea 39294-79-6, Seractide acetate 39324-30-6, Pepstatin 39325-01-4, Picibanil 39562-70-4, Nitrendipine 39624-65-2, Azanator maleate 39624-66-3, Trepipam maleate 39698-78-7, Saralasin acetate 39791-20-3, Nylestriol 39809-25-1, Penciclovir 39878-70-1, Talampicillin hydrochloride 40034-42-2, Rosoxacin 40054-69-1, Etizolam 40180-04-9, Ticrynafen 40391-99-9, Pamidronic acid 40507-23-1, Fluproquazone 40594-09-0, Flucindole 40691-50-7, Tixanox 40759-33-9, Nolinium bromide 40796-97-2, Bemesetron 40819-93-0, Lorajmine hydrochloride 40828-44-2, Clazolimine 40828-45-3, Azolimine 40828-46-4, Suprofen 40966-79-8, Sarpicillin 41020-67-1, Mexrenoate potassium 41020-79-5, Dicirenone 41078-02-8, Enprofylline 41094-88-6, Tracazolate 41113-86-4, Bromoxanide 41147-04-0, Xanoxate sodium 41340-25-4, Etodolac 41570-61-0, Tulobuterol 41575-94-4, Carboplatin 41692-24-4 41708-72-9, Tocainide 41729-52-6, Dezaguanine 41767-29-7, Fluocortin butyl 41859-67-0, Bezafibrate 41927-88-2, sodium iodide 123 41964-07-2, Tolimidone 41992-22-7, Spirogermanium hydrochloride 42021-34-1, Biriperone 42045-97-6, Phenaridine 42116-76-7, Carnidazole 42116-77-8 42200-33-9, Nadolol 42220-21-3, iodocholesteroli131 42281-59-4, Oxilorphan 42408-78-6, Pirandamine hydrochloride 42408-82-2, Butorphanol 42422-68-4, Taleranol 42461-78-9, Sulfonterol hydrochloride 42616-25-1, Methioninase 42779-82-8, Clopirac 42794-76-3, Midodrine 42835-25-6, Flumequine 42864-78-8, Bevantolol hydrochloride 42877-18-9, Pelanserin hydrochloride 42879-47-0, Pranolium chloride 42924-53-8, Nabumetone 42971-09-5, Vinpocetine 43033-72-3, Levomethadyl acetate hydrochloride 43143-11-9, Bispyrithione magsulfex 43200-80-2, Zopiclone 43210-67-9, Fenbendazole 47141-42-4, Levobunolol 49562-28-9, Fenofibrate 49637-08-3, Nabitan hydrochloride 49697-38-3, Rimexolone 49755-67-1, Ioglicic acid 49763-96-4, Stiripentol 49780-10-1, Azaclorzine hydrochloride 49847-97-4, Prorenoate potassium 50264-69-2, Lonidamine 50370-12-2, Cefadroxil 50528-97-7, Xilobam 50650-76-5, Piroctone 50673-97-7, Colestolone 50679-07-7, Cinepazet maleate 50679-08-8, Terfenadine 50700-72-6, Vecuronium bromide 50708-95-7, Tinabinol 50838-36-3, Tolciclate 50847-11-5, Ibudilast 50924-49-7, Mizoribine 51022-71-0, Nabilone 51022-73-2, Zometapine 51022-74-3, Iotroxic acid 51022-75-4, Cliprofen 51022-76-5, Sulnidazole 51022-98-1, Butirosin sulfate 51025-85-5, Arbekacin 51222-36-7, Ciclafrine hydrochloride 51222-37-8, Iproxamine hydrochloride 51234-28-7, Benoxaprofen 51264-14-3, Amsacrine 51321-79-0, Sparfosic acid 51333-22-3, Budesonide 51354-31-5, Nisterime acetate 51384-51-1, Metoprolol 51481-61-9, Cimetidine 51481-63-1, Bucainide maleate 51481-65-3, Mezlocillin 51481-67-5, Octriptyline phosphate 51598-60-8, Cimetropium bromide 51627-14-6, Cefatrizine 51627-20-4, Cefaparole 51762-05-1, Cefroxadine 51764-33-1, Iodoxamate meglumine 51773-92-3, Mefloquine hydrochloride 51781-06-7, Carteolol 51781-21-6, Carteolol hydrochloride 51876-98-3, Gliamilide 51876-99-4, Ioseric acid 52123-49-6, Cefazaflur sodium 52128-35-5, Trimetrexate 52212-02-9, Pipecuronium bromide 52214-84-3, Ciprofibrate 52279-58-0, Metogest 52279-59-1, Moxnidazole 52365-63-6, Dipivefrin 52389-27-2, Dexclamol hydrochloride 52468-60-7, Flunarizine 52618-68-5, Tioperidone hydrochloride 52645-53-1, Permethrin 52663-86-2 52760-47-1, Tametraline hydrochloride 52794-97-5, Carubicin hydrochloride 53066-26-5, Lexithromycin 53123-88-9, Sirolimus 53152-21-9, Buprenorphine hydrochloride 53179-07-0, Nisoxetine 53179-10-5, Fluperamide 53179-12-7, Clopimozide 53179-13-8, Pirfenidone 53267-01-9, Cibenzoline 53361-24-3, Imafen hydrochloride 53400-68-3, Tiquinamide hydrochloride 53583-79-2, Sultopride 53597-26-5, Etoformin hydrochloride 53597-27-6, Fendosal 53597-28-7, Fludazonium chloride 53643-48-4, Vindesine 53648-55-8, Dezocine 53714-56-0, Leuprolide 53716-45-3, Anilopam hydrochloride 53716-47-5, Nexeridine hydrochloride 53716-49-7, Carprofen 53716-50-0, Oxfendazole 53736-52-0, Cromitrile sodium 53808-87-0, Tetroxoprim 53808-88-1, Lonazolac 53902-12-8, Tranilast 53910-25-1, Pentostatin 53983-00-9, Nibroxane 53994-73-3, Cefaclor 54024-22-5, Desogestrel

54048-10-1, Etonogestrel 54081-68-4, Vinleurosine sulfate 54120-61-5, Prostalene 54143-54-3, Sepazonium chloride 54143-55-4, Flecainide 54182-58-0, Sucralfate 54182-60-4 54194-00-2, Salcolex 54239-37-1, Cimaterol 54350-48-0, Etretinate 54504-70-0, Theofibrate 54527-84-3, Nicardipine hydrochloride 54573-75-0, 1α-hydroxyvitamin D2 54605-45-7, Iocarmate meglumine 54644-15-4 54739-18-3, Fluvoxamine 54767-75-8, Suloctidil 54824-17-8, Mitonafide 54910-89-3, Fluoxetine 54965-22-9, Fluspiperone 55028-70-1, Arbaprostil 55028-71-2, Fluprostenol sodium 55028-72-3 55096-26-9, Nalmefene 55134-13-9, Narasin 55142-85-3, Ticlopidine 55149-05-8, Pirolate 55162-26-0, Pirbenicillin sodium 55242-55-2, Propentofylline 55242-74-5, Oxifungin hydrochloride 55242-77-8, Triafungin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release active ingredients)

IT 55268-75-2, Cefuroxime 55294-15-0, Muzolimine 55298-68-5, Neomycin palmitate 55453-87-7, Isoxepac 55560-96-8, Tixocortol pivalate 55694-87-6, Pentizidone sodium 55695-56-2, Cloroperone hydrochloride 55721-11-4, Secalciferol 55774-33-9, Azathioprine sodium 55779-18-5, Arprinocid 55837-27-9, Piretanide 55837-29-1, Tiropramide 55870-64-9, Pentisomicin 55881-07-7, Miokamycin 55905-53-8, Clebopride 55981-09-4, Nitazoxanide 56030-54-7, Sufentanil 56049-88-8, Indacrinone 56079-80-2, Ropitoin hydrochloride 56093-45-9, Selenium sulfide 56119-96-1, Furodazole 56187-89-4, Ximoprofen 56208-01-6, Pifarnine 56211-40-6, Torasemide 56219-57-9, Arildone 56281-36-8, Motretinide 56290-94-9, Medroxalol 56383-05-2, Zindotrine 56391-55-0, Octazamide 56391-57-2, Netilmicin sulfate 56420-45-2, Epirubicin 56430-99-0, Flumecinol 56470-64-5, Anordrin 56605-16-4D, Spiromustine, di-Ph derivs. 56611-65-5, Oxagrelate 56689-42-0, Repromicin 56689-44-2, Nitramisole hydrochloride 56717-18-1, Isotiquimide 56741-95-8, Bropirimine 56784-39-5, Ozolinone 56796-20-4, Cefmetazole 56917-29-4, Fluretofen 56980-93-9, Celiprolol 56995-20-1, Flupirtine 57010-32-9, Tiapamil hydrochloride 57041-67-5, Desflurane 57067-46-6, Isamoxole 57109-90-7, Clorazepate dipotassium 57149-07-2, Naftopidil 57166-13-9, Napactadine hydrochloride 57248-88-1, Pamidronate disodium 57262-94-9, Setiptiline 57285-09-3, Folliculostatin 57381-26-7, Irsogladine 57432-61-8, Methylergonovine maleate 57441-90-4, Nivimedone sodium 57540-79-1, Nisbuterol mesylate 57645-05-3, Sermetacin 57653-26-6, Fenobam 57666-60-1, Nitrafudam hydrochloride 57726-65-5, Nufenoxole 57773-63-4, Triptorelin 57773-65-6, Deslorelin 57775-22-1, Etoperidone hydrochloride 57781-15-4, Halopredone 57801-81-7, Brotizolam 57808-65-8, Closantel 57982-78-2, Budipine 57998-68-2, Diaziquone 58019-50-4, Menabitan hydrochloride 58019-65-1, Nabazenil 58066-85-6, Miltefosine 58152-03-7, Isepamicin 58167-78-5, Tandamine hydrochloride 58239-89-7, Moxazocine 58261-91-9, Mefenidil 58473-74-8, Cinromide 58493-49-5, Olvanil 58497-00-0, Procinonide 58503-79-0, Meobentine sulfate 58524-83-7, Ciprocinonide 58525-82-9, Azatyrosine 58581-89-8, Azelastine 58712-69-9, Traxanox 58795-03-2, Apalcillin sodium 58934-46-6, Lorcainide hydrochloride 58944-73-3, Sinefungin 58957-92-9, Idarubicin 58970-76-6, Ubenimex 59017-64-0, Ioxaglic acid 59018-13-2 59070-06-3, Ticarcillin cresyl sodium 59122-46-2, Misoprostol 59160-29-1, Lidofenin 59170-23-9, Bevantolol 59179-95-2, Lorzafone 59227-89-3, Laurocapram 59263-76-2, Meptazinol hydrochloride 59333-90-3, Exaprolol hydrochloride 59467-96-8, Midazolam hydrochloride 59497-39-1, Naflocort 59653-73-5, Teroxirone 59703-84-3, Piperacillin sodium 59729-33-8, Citalopram 59733-86-7, Butikacin 59756-39-7, Enolicam sodium 59794-18-2, Paulomycin 59803-98-4, Brimonidine 59804-37-4, Tenoxicam 59831-63-9, Doconazole 59831-64-0, Milenperone 59831-65-1, Halopemide 59917-39-4, Vindesine sulfate 59937-28-9, Malotilate 59954-01-7, Pamatolol sulfate 60019-19-4, Iotetric acid 60050-95-5, Sulfoxamine 60084-10-8, Tiazofurin 60086-22-8, Clopipazan mesylate 60135-22-0, Flumoxonide 60142-96-3, Gabapentin 60166-93-0, Iopamidol 60200-06-8, Clorsulon 60207-31-0, Azaconazole 60209-20-3, Lycetamine 60282-87-3, Gestodene 60325-46-4, Sulprostone 60398-23-4, Iodoamiloride 60400-92-2, Proxicromil 60525-15-7, Zimelidine hydrochloride 60560-33-0, Pinacidil 60569-19-9, Propiverine 60607-34-3, Oxatomide 60607-35-4, Topterone 60628-96-8, Bifonazole 60653-25-0, Orpanoxin 60719-84-8, Amrinone 60719-85-9, Ciprefadol

succinate 60762-57-4, Pirlindole 60857-08-1, Prostratin 60925-61-3, Ceforanide 60940-34-3, Ebselen 60976-05-8 61036-62-2, Teicoplanin 61177-45-5, Clavulanate potassium 61220-69-7, Tiopinac 61260-05-7, Prenalterol hydrochloride 61263-35-2, Meteneprost 61270-78-8, Cefonicid sodium 61318-91-0, Sulconazole nitrate 61325-80-2, Flumezapine 61379-65-5, Rifapentine 61380-27-6, Carfentanil citrate 61380-41-4, Lofentanil oxalate 61413-54-5, Rolipram 61444-62-0, Nifluridide 61477-94-9, Pirmenol hydrochloride 61481-30-9, Dicranin 61484-39-7, Pareptide sulfate 61489-71-2, Menotropin 61570-90-9, Tioxidazole 61622-34-2, Cefotiam 61825-94-3, Oxaliplatin 61849-14-7, Epoprostenol sodium 61869-08-7, Paroxetine 62013-04-1, Dirithromycin 62087-72-3, Pentigetide 62134-34-3, Butoprozine hydrochloride 62220-58-0, Bipenamol hydrochloride 62265-68-3, Quinfamide 62304-98-7, Thymalfasin 62435-42-1, Perfosfamide 62488-57-7 62571-86-2, Captopril 62571-87-3, Minaxolone 62587-73-9, Cefsulodin 62613-82-5, Oxiracetam 62625-19-8, Pirogliride tartrate 62658-63-3, Bopindolol 62666-20-0, Progabide 62732-44-9, Ipidacrine 62816-98-2, Ormaplatin 62851-43-8, Zidometacin 62893-20-3, Cefoperazone sodium 62928-11-4, Iproplatin 62929-91-3, Procaterol hydrochloride 62973-76-6, Azanidazole 62973-77-7, Parconazole hydrochloride 62989-33-7, Sapropterin 62996-74-1, Staurosporine 63119-27-7, Anitrazafen 63198-97-0, Viroxime 63204-23-9, Oxmetidine hydrochloride 63245-28-3, Etifenin 63251-39-8, Sulfinalol hydrochloride 63269-31-8, Ciramadol 63358-49-6, Aspoxicillin 63534-64-5, Iosulamide meglumine 63585-09-1, Foscarnet sodium 63590-19-2, Balanol 63590-64-7, Terazosin 63612-50-0, Nilutamide 63659-18-7, Betaxolol 63659-19-8, Betaxolol hydrochloride 63675-72-9, Nisoldipine 63774-77-6, Somatomedin B 63941-73-1, Ioglucol 63941-74-2, Ioglucomide 63950-06-1, Esorubicin hydrochloride 64019-93-8, Dipivefrin hydrochloride 64059-66-1, Cetaben sodium 64063-83-8, Picotrin diolamine 64092-48-4, Zomepirac sodium 64211-45-6, Oxiconazole 64221-86-9, Imipenem 64228-81-5, Atracurium besylate 64318-79-2, Gemeprost 64379-93-7, Cinflumide 64420-40-2, Etibendazole 64461-82-1, Tizanidine hydrochloride 64485-93-4, Cefotaxime sodium 64706-54-3, Bepridil 64808-48-6, Lobenzarit sodium 64872-77-1, Butoconazole nitrate 64924-67-0, Halofuginone hydrobromide 64953-12-4, Moxalactam disodium 65009-35-0, Lidamidine hydrochloride 65043-22-3, Indeloxazine hydrochloride 65052-63-3, Cefetamet 65057-90-1, Talisomycin 65093-40-5, Cytarabine ocfosfate 65141-46-0, Nicorandil 65222-35-7, Pazelliptine 65271-80-9, Mitoxantrone 65277-42-1, Ketoconazole 65322-72-7, Endralazine mesylate 65454-13-9, Lateritin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release active ingredients)

IT 65473-14-5, Naftifine hydrochloride 65511-42-4, Nantradol hydrochloride 65573-02-6, Impromidine hydrochloride 65646-68-6, Fenretinide 65652-44-0, Pirbuterol acetate 65717-97-7, Disofenin 65807-02-5, Goserelin 65847-85-0, Morniflumate 65886-71-7, Fazarabine 65899-73-2, Tioconazole 65928-58-7, Dienogest 65950-99-4, Pirquinozol 66085-59-4, Nimodipine 66104-22-1, Pergolide 66108-95-0, Iohexol 66148-78-5, Temocillin 66172-75-6, Verofylline 66195-31-1, Ibopamine 66292-52-2, Butilfenin 66292-53-3, Iprofenin 66357-35-5, Ranitidine 66357-59-3, Zantac 66364-74-7, Enpiroline phosphate 66504-75-4, Bicifadine hydrochloride 66537-94-8, Cyproximide 66564-14-5, Cinitapride 66569-27-5, Sparfosate sodium 66575-29-9, Colforsin 66608-04-6, Rolgamidine 66635-85-6, Anirolac 66711-21-5, Apraclonidine 66722-44-9, Bisoprolol 66734-12-1, Butopamine 66849-34-1, Dexifosfamide 66852-54-8, Halobetasol propionate 66887-96-5, Propikacin 66898-60-0, Talosalate 66898-62-2, Talniflumate 66960-35-8, Metkephamid acetate 66969-81-1, Tiodazosin 67102-87-8, Pentomone 67227-55-8, Primidolol 67227-56-9, Fenoldopam 67337-44-4, Sarmoxicillin 67394-31-4, Verilopam hydrochloride 67422-14-4, Proinsulin (human) 67450-45-7, Eclanamine maleate 67489-39-8, Talmetacin 67699-41-6, Vinzolidine sulfate 67700-30-5, Furaprofen 67763-96-6, Somatomedin C 67832-40-0, Malethamer 67915-31-5, Terconazole 67992-58-9 68099-86-5, Bepridil hydrochloride 68252-19-7, Pirmenol 68284-69-5, Disobutamide 68291-97-4, Zonisamide 68302-57-8, Amlexanox 68307-81-3, Trioxifene mesylate 68367-52-2, Sorbinil 68377-92-4, Arotinolol 68379-03-3, Clofilium phosphate

68401-82-1, Ceftizoxime sodium 68475-42-3, Anagrelide 68506-86-5, Vigabatrin 68616-83-1, Pentamorphone 68630-75-1, Buserelin acetate 68681-42-5, Tonazocine mesylate 68693-11-8, Modafinil 68693-30-1, Somantadine hydrochloride 68741-18-4, Buterizine 68813-55-8, Oxantel pamoate 68844-77-9, Astemizole 68902-57-8, Metioprim 69014-14-8, Tiotidine 69049-73-6, Nedocromil 69123-90-6, Fiacitabine 69123-98-4, Fialuridine 69207-52-9, Methyl palmoxirate 69365-67-9, Fenoctimine sulfate 69372-19-6, Pemirolast 69376-27-8, Dextrorphan hydrochloride 69381-94-8, Fenprostalene 69388-79-0, Sulbactam pivoxil 69402-03-5, Piridicillin sodium 69425-13-4, Prifelone 69429-85-2, Cilobamine mesylate 69598-75-0, Complestatin 69648-38-0, Butaprost 69655-05-6, Didanosine 69712-56-7, Cefotetan 69739-16-8, Cefodizime 69756-53-2, Halofantrine 69815-39-0, Proxorphan tartrate 69839-83-4, Didox 69900-72-7, Trimoprostil 70018-51-8, Quazinone 70052-12-9, Eflornithine 70169-80-1, Lofemizole hydrochloride 70222-86-5, Levonantradol hydrochloride 70288-86-7, Ivermectin 70374-27-5, Lomoxicam 70374-39-9, Lornoxicam 70384-29-1, Peplomycin sulfate 70384-91-7, Lortalamine 70458-92-3, Pefloxacin 70458-96-7, Norfloxacin 70529-35-0, Itazigrel 70590-58-8, Etrabamine 70641-51-9, Edelfosine 70704-03-9, Vinconate 70724-25-3, Carbazeran 70775-75-6, Octenidine hydrochloride 70788-28-2, Flurofamide 70788-29-3, Tolfamide 70797-11-4, Cefpiramide 70801-02-4, Flutroline 70865-14-4, Conorphone hydrochloride 70891-37-1, Nafimidone hydrochloride 70895-39-5, Tipropidil hydrochloride 70931-18-9, Isofloxythepin 71002-09-0, Pirazolac 71119-11-4, Bucindolol 71144-97-3, Probicromil calcium 71251-04-2, Surfomer 71276-44-3, Quadazocine mesylate 71294-60-5, Rohitukine 71320-77-9, Moclobemide 71351-79-6, Icotidine 71486-22-1, Vinorelbine 71522-58-2, Forfenimex 71576-41-5, Aptazapine maleate 71628-96-1, Menogaril 71653-63-9, Riodipine 71675-85-9, Amisulpride 71678-03-0, Illimaquinone 71767-13-0, Iotasul 71807-56-2, Etintidine hydrochloride 72238-02-9D, Retelliptine, demethylated 72275-67-3, Astromicin sulfate 72301-78-1, Zinviroxime 72301-79-2, Enviroxime 72318-55-9, Indorenate hydrochloride 72324-18-6, Stepronin 72432-03-2, Miglitol 72432-10-1, Aniracetam 72479-26-6, Fenticonazole 72481-99-3, Brocrinat 72496-41-4, Pirarubicin 72509-76-3, Felodipine 72558-82-8, Ceftazidime 72559-06-9, Rifabutin 72573-82-1, Gadoteric acid 72629-69-7, Sarcophytol A 72702-95-5, Ponalrestat 72732-56-0, Piritrexim 72741-87-8, Swainsonine 72797-41-2, Tianeptine 72803-02-2, Darodipine 72808-81-2, Tepirindole 72822-12-9, Dapiprazole 72895-88-6, Eltenac 72956-09-3, Carvedilol 73080-51-0, Repirinast 73105-03-0, Pentamustine 73196-97-1, Dactimicin 73205-13-7, Ticabesone propionate 73218-79-8, Apraclonidine hydrochloride 73231-34-2, Florfenicol 73247-43-5, Gonadocrinin 73264-44-5, Sucrosofate potassium 73334-07-3, Iopromide 73384-59-5, Ceftriaxone 73514-87-1, Fosarilate 73573-87-2, Formoterol 73590-58-6, Omeprazole 73647-73-1, Viprostol 73681-12-6, Indecainide hydrochloride 73747-21-4, Naboctate hydrochloride 73771-04-7, Prednicarbate 73793-66-5, Prizidilol hydrochloride 73803-48-2, Tripamide 73899-76-0, Diacetolol hydrochloride 73963-72-1, Cilostazol 74011-58-8, Enoxacin 74014-51-0, Rokitamycin 74050-98-9, Ketanserin 74103-06-3, Ketorolac 74129-03-6, Tebuquine 74149-70-5, Parabactin 74150-27-9, Pimobendan 74226-22-5, Dazoxiben hydrochloride 74381-53-6, Leuprolide acetate 74434-21-2, Cucumarioside 74513-62-5, Trimegestone 74559-85-6, Zenazocine mesylate 74639-40-0, Docarpamine 74711-43-6, Zaltoprofen 74738-24-2, Recainam 74752-07-1, Recainam hydrochloride 74772-77-3, Ciglitazone 74790-08-2, Spiroplatin 74863-84-6, Argatroban 75067-66-2, Bromperidol decanoate 75176-37-3, Zofenoprilat 75219-46-4, Atrimustine 75330-75-5, Lovastatin 75358-37-1, Linogliride 75438-57-2, Moxonidine 75444-64-3, Flumeridone 75444-65-4, Pirenperone 75530-68-6, Nilvadipine 75564-40-8, Biclodil hydrochloride 75607-67-9, Fludarabine phosphate 75659-08-4, Dilevalol hydrochloride 75689-38-2, Piquindone hydrochloride 75695-93-1, Isradipine 75696-02-5, Cinolazepam 75733-50-5, Pramiracetam hydrochloride 75738-58-8, Cefmenoxime hydrochloride 75751-89-2, Iogulamide 75847-73-3, Enalapril 75859-03-9, Rimcazole hydrochloride 75889-62-2, Fostedil 75957-60-7, Splenopentin 75991-49-0, Dazepinil hydrochloride 76053-16-2, Reclazepam 76144-81-5, Mildronate 76168-82-6, Ramoplanin 76263-13-3, Fluzinamide 76301-19-4, Timefurone 76420-72-9, Enalaprilat 76448-47-0, Veradoline hydrochloride 76470-66-1, Loracarbef

76497-13-7, Sultamicillin 76535-71-2, Suproclone
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release active ingredients)

IT 76541-72-5, Mifobate 76547-98-3, Lisinopril 76568-02-0, Flosequinan
76584-70-8, Depakote 76610-84-9, Cefbuperazone 76712-82-8, Histrelin
76824-35-6, Famotidine 76894-77-4, Dazmegrel 76932-56-4, Nafarelin
76963-41-2, Axid 76990-56-2, Milacemide 77016-85-4, Plomestane
77086-22-7, Dizocilpine maleate 77164-20-6, Levomoprolol 77181-69-2,
Sorivudine 77257-42-2, Stilonium iodide 77287-05-9, Rioprostil
77287-90-2, Xorphanol mesylate 77327-05-0, Didemnin B 77590-95-5,
Cetamolol hydrochloride 77590-96-6, Flordipine 77590-97-7, Fluradoline
hydrochloride 77599-17-8, Panomifene 77671-31-9, Enoximone
77679-27-7 77858-21-0, Velaresol 78013-07-7, Bactobolamine
78040-85-4, Coumermycin 78110-38-0, Aztreonam 78113-36-7, Romurtide
78186-33-1, Fumoxicillin 78186-34-2, Bisantrene 78266-06-5, Mebrofenin
78273-80-0, Roxatidine 78299-53-3, Tiacrilast 78308-51-7 78371-66-1,
Bucromarone 78415-72-2, Milrinone 78613-35-1, Amorolfine 78649-41-9,
Iomeprol 78755-81-4, Flumazenil 78822-40-9, Pirlimycin hydrochloride
78860-34-1, (L-783281) 78919-13-8, Iloprost 78967-07-4, Mofezolac
78994-23-7, Levormeloxifene 79094-20-5, Daltroban 79201-85-7,
Picenadol 79211-34-0, Iotriside 79217-60-0, Cyclosporin 79350-37-1,
Cefixime 79404-91-4, Cilofungin 79498-31-0, Glaucocalyxin A
79516-68-0, Levocabastine 79578-14-6, Timobesone acetate 79617-96-2,
Sertraline 79619-32-2, Flavodilol maleate 79660-72-3, Fleroxacin
79672-88-1, Piriprost 79712-53-1, Tazifylline hydrochloride
79770-24-4, Iotrolan 79778-41-9, Neridronic acid 79794-75-5,
Loratadine 79798-39-3, Ketorfanol 79831-76-8, Castanospermine
79874-76-3, Delmopinol 79902-63-9, Simvastatin 80018-06-0, Fengabine
80125-14-0, Remoxipride 80168-44-1, Zinoconazole hydrochloride
80195-36-4, Cefdaloxime 80214-83-1, Roxithromycin 80263-73-6,
Eclazolast 80343-63-1, Sufotidine 80410-37-3, Fezolamine fumarate
80433-71-2, Levoleucovorin calcium 80451-05-4, Cecropin B 80474-14-2,
Fluticasone propionate 80486-69-7, Cloticasone propionate 80573-04-2,
Balsalazide 80576-83-6, Edatrexate 80621-81-4, Rifaximin 80755-51-7,
Bunazosin 80809-81-0, Docebenone 80828-32-6, Indolapril hydrochloride
80841-47-0, Asulacrine 80879-63-6, Emiglitate 80880-90-6, Telenzepine
80883-55-2, Enviradene 81026-63-3, Enisoprost 81045-50-3, Pivopril
81093-37-0, Pravastatin 81098-60-4, Propulsid 81103-11-9,
Clarithromycin 81129-83-1, Cilastatin sodium 81131-70-6, (Pravachol)
81161-17-3, Esmolol hydrochloride 81167-22-8, Imiloxan hydrochloride
81329-71-7, Modecainide 81377-02-8, L 363586 81382-52-7, Pentiapine
maleate 81424-67-1, Caracemide 81435-67-8, Losulazine hydrochloride
81447-80-5, Diprafenone 81447-81-6, Bromadoline maleate 81525-10-2,
Nafamostat 81669-57-0, Anistreplase 81732-65-2, Bambuterol
81737-62-4, Bendacalol mesylate 81801-12-9, Xamoterol 81840-15-5,
Vesnarinone 81845-44-5, Ciprostene 81907-78-0, Batebulast
81938-43-4, Zofenopril calcium 81957-25-7, Dazopride fumarate
81965-43-7, Sarcnu 82030-87-3, Somatrem 82101-10-8, Flerobuterol
82186-77-4, Benflumetol 82230-03-3, Carbetimer 82230-53-3, Girisopam
82239-52-9, Moxiraprine 82248-59-7, Tomoxetine hydrochloride
82410-32-0, Ganciclovir 82419-36-1, Ofloxacin 82547-58-8, Cefteram
82571-53-7, Ozagrel 82626-48-0, Zolpidem 82664-20-8, Flurithromycin
82707-54-8, Neutral endopeptidase 82708-31-4, Oocyte maturation
inhibitor 82752-99-6, Nefazodone hydrochloride 82768-85-2, Quinaprilat
82834-16-0, Perindopril 82855-09-2D, Combretastatin, analogs
82857-82-7, Ilepcimide 82924-03-6, Pentopril 82964-04-3, Tolrestat
82989-25-1, Tazanolast 83059-56-7, Zabicipril 83086-73-1, Tubulozole
hydrochloride 83150-76-9, Octreotide 83166-18-1, Tampramine fumarate
83198-90-7, Tiprinast meglumine 83200-11-7, Vinepidine sulfate
83435-66-9, Delapril 83435-67-0, Delapril hydrochloride 83462-55-9,
Deoxypyridinoline 83519-04-4, Ilmofosine 83529-09-3, Ciladopa
hydrochloride 83602-05-5, Spiraprilat 83646-97-3, Inocoterone
83688-84-0, Tertatolol 83784-18-3, Lutrelin acetate 83799-24-0,
Fexofenadine 83805-11-2, Flocalcitriol 83863-79-0, Florifenine
83881-51-0, Cetirizine 83898-67-3, Mioflazine hydrochloride
83905-01-5, Azithromycin 83928-76-1, Gepirone 83997-75-5,
Iododoxorubicin 84057-84-1, Lamotrigine 84057-95-4, Ropivacaine
84088-42-6, Roquinimex 84166-17-6, Fenprinast hydrochloride

84203-09-8, Trifenagrel 84290-27-7, Tucaresol 84305-41-9, Cefminox
84371-65-3, Mifepristone 84379-13-5, Bretazenil 84392-17-6, Xenalipin
84408-37-7, Desciclovir 84412-94-2, Ruboxyl 84449-90-1, Raloxifene
84485-00-7, Sibutramine hydrochloride 84490-12-0, Piroximone
84611-23-4, Erdosteine 84625-61-6, Itraconazole 84845-57-8, Ritipenem
84845-75-0, Niperotidine 84880-03-5, Cefpimizole 84957-29-9, Cefpirome
85053-47-0, Suricainide maleate 85068-76-4 85118-44-1, Minocromil
85136-71-6, Tilisolol 85175-67-3, Zatebradine 85181-38-0, Tropanserin
hydrochloride 85197-77-9, Tipredane 85202-17-1, Stobadine 85216-79-1
85441-61-8, Quinapril 85465-82-3, Thymotrinan 85468-01-5, Gusperimus
trihydrochloride 85622-93-1, Temozolomide 85650-52-8, Mirtazapine
85666-17-7, Furegrelate sodium 85683-41-6, Metipamide 85691-74-3,
Pirmagrel 85721-33-1, Ciprofloxacin 85798-08-9, Quinpirole
hydrochloride 85969-07-9, Budotitane 85977-49-7, Tauromustine
86015-38-5, Neflumozide hydrochloride 86042-50-4, Cistinexine
86048-40-0, Quazolast 86050-77-3, Gadopentetate dimeglumine
86116-60-1, Azaloxan fumarate 86160-82-9, Lavoltidine succinate
86181-42-2, Temelastine 86386-73-4, Fluconazole 86433-40-1,
Terflavoxate 86487-64-1, Setoperone 86541-74-4, Benazepril
hydrochloride 86541-78-8, Benazeprilat 86780-90-7, Aranidipine
86828-07-1, Mallotojaponin 86832-68-0, Carumonam sodium 86914-11-6,
Tolgabide 87005-03-6, Panaxytriol 87051-43-2, Ritanserin 87056-78-8,
Quinagolide 87071-16-7, Arclofenin 87173-97-5, Spiradoline mesylate
87233-61-2, Emedastine 87239-81-4, Cefpodoxime proxetil 87248-13-3,
Vapiprost hydrochloride 87333-19-5, Ramipril 87359-33-9, Isomazole
hydrochloride 87495-31-6, Disoxaril 87495-33-8, Napamezole
hydrochloride 87573-01-1, Salnacedin 87638-04-8, Carumonam
87679-37-6, Trandolapril 87691-92-7, Tiospirone hydrochloride
87719-32-2, Etarotene
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release
active ingredients)

IT 87726-17-8, Panipenem 87760-53-0, Tandospirone 87771-40-2, Ioversol
87784-12-1, Ofornine 87806-31-3, Porfimer sodium 87810-56-8,
Fostriecin 87936-82-1, Tazadolene succinate 88040-23-7, Cefepime
88069-67-4, Pilsicainide 88107-10-2, Tomelukast 88133-11-3,
Bemitradine 88150-42-9, Amlodipine 88296-61-1, Medorinone
88296-62-2, Transcainide 88303-60-0, Losoxantrone 88430-50-6,
Beraprost 88637-37-0, Diphenhydramine citrate 88669-04-9,
Trospectomycin 88768-40-5, Cilazapril 88844-73-9, Flestolol sulfate
89194-77-4, Bisaramil 89198-09-4, Imazodan hydrochloride 89213-87-6,
Carperitide 89226-50-6, Manidipine 89232-84-8, Pelrinone hydrochloride
89303-64-0, Atiprosin maleate 89365-50-4, Salmeterol 89371-37-9,
Imidapril 89383-13-1, Somidobove 89419-40-9, Mosapramine 89565-68-4,
Tropisetron 89651-00-3, Voxergolide 89667-40-3, Isbogrel 89672-11-7,
Cioteronel 89778-26-7, Toremifene 89786-04-9, Tazobactam 89797-00-2,
Iopentol 89943-82-8, Cicletanine 89987-06-4, Tiludronic acid
90055-97-3, Tienoxolol 90182-92-6, Zacopride 90243-66-6, Montirelin
90274-23-0, Zaltidine hydrochloride 90293-01-9, Bifemelane 90357-06-5,
Bicalutamide 90729-41-2, Oxodipine 90729-43-4, Ebastine 90733-42-9,
Edifolone acetate 90779-69-4, Atosiban 90849-08-4, Oximonam sodium
90850-05-8, Gloximonam 90898-90-1, Oximonam 90996-54-6, Rhizoxin
91077-32-6, Dezinamide 91161-71-6, Terbinafine 91296-86-5, Difloxacin
hydrochloride 91296-87-6, Sarafloxacin hydrochloride 91374-21-9,
Ropinirole 91406-11-0, Esuprone 91431-42-4, Lonapalene 91524-15-1,
Irloxacin 91524-18-4, Azumolene sodium 91587-01-8, Pelretin
91618-36-9, Ibafloxacin 91714-94-2, Bromfenac 91832-40-5, Cefdinir
92047-76-2, Tetrachlorodecaoxide 92118-27-9, Fotemustine 92236-42-5,
Glutapyrone 92339-11-2, Iodixanol 92623-84-2, Pravadoline maleate
92623-85-3, Milnacipran 92665-29-7, Cefprozil 92788-10-8, Rogletimide
92803-82-2, Aphidicolin glycinate 92812-82-3, fluorodopaf18
92817-10-2, 16-α-Fluoroestradiol 93047-39-3, Etanterol
93135-89-8, Methoxatone 93221-48-8, Levobetaxolol 93390-81-9,
Fosphenytoin 93413-69-5, Venlafaxine 93479-97-1, Glimepiride
93738-40-0, Ralitoline 93957-54-1, Fluvastatin 93957-55-2, Fluvastatin
sodium 94079-80-8, Cicaprost 94168-98-6, Rifametane 94535-50-9,
Levcromakalim 94651-09-9, Cicloprolol 94739-29-4, Lemildipine
94820-09-4, Cadexomer iodine 94841-17-5, Spirapril hydrochloride
95058-81-4, Gemcitabine 95153-31-4, Perindoprilat 95190-13-9,

Tetrazolast meglumine 95232-68-1, Tenosal 95233-18-4, Atovaquone 95399-71-6, Fosinoprilat 95522-45-5, Colestimide 95635-55-5, Ranolazine 95671-26-4, Tipentosin hydrochloride 95733-03-2, Daphnodorin A 95734-82-0, Nedaplatin 95847-70-4, Ipsapirone 95896-08-5, Anaritide 96036-03-2, Meropenem 96128-92-6, Clentiazem maleate 96201-88-6, Brequinar sodium 96301-34-7, Atamestane 96346-61-1, Onapristone 96389-68-3, Crisnatol 96392-96-0, Dexormaplatin 96449-05-7, Rispenzepine 96604-21-6, Ocinaplon 96609-16-4, Lifibrol 96736-12-8 96829-58-2, Orlipastat 96892-57-8, Hepsulfam 96946-42-8, Cisatracurium besilate 97048-13-0, Urofollitropin 97068-30-9, Elsamitrucin 97240-79-4, Topiramate 97322-87-7, Troglitazone 97519-39-6, Ceftibuten 97534-21-9, Merbarone 97548-97-5, Quinelorane hydrochloride 97682-44-5, Irinotecan 97772-98-0, Butedronate tetrasodium 97919-22-7 97938-30-2, Vexibinol 97964-56-2, Lorglumide 98048-97-6, Fosinopril 98079-51-7, Lomefloxacin 98116-53-1, Sulukast 98206-10-1, Flesinoxan 98319-26-7, Finasteride 98383-18-7, Ecomustine 98449-05-9, Butixocort propionate 98569-62-1, Mallotochromene 98631-95-9, Sobuzoxane 99009-20-8, Pyrazoloacridine 99011-02-6, Imiquimod 99107-52-5, Bunaprolast 99149-95-8, Saruplase 99156-66-8, Barmastine 99248-33-6, Seglitide acetate 99258-56-7, Oxamisole 99283-10-0, Molgramostim 99287-30-6, Egualen 99291-25-5, Levodropropizine 99294-94-7, Teriparatide acetate 99464-64-9, Ampiroxicam 99519-84-3, Carboxyamidotriazole 99592-32-2, Sertaconazole 99614-02-5, Ondansetron 99665-00-6, Flomoxef 99705-65-4, Naxagolide hydrochloride 99759-19-0, Tiqueside 99821-44-0, Nasaruplase 100188-33-8, Piridronate sodium 100324-81-0, Lisofylline 100427-26-7, Lercanidipine 100490-36-6, Tosufloxacin 100643-96-7, Indolidan 100981-43-9, Ebrotidine 100986-85-4, Levofloxacin 101001-34-7, Pamicogrel 101246-66-6, Phenserine 101246-68-8, Eptastigmine 101363-10-4, Rufloxacin 101477-55-8, Lomerizine 101526-83-4, Sematilide 101530-10-3, Lanoconazole 101828-21-1, Butenafine 102394-31-0, Otenzepad 102396-24-7, Jasplakinolide 102426-96-0, Paldimycin 102583-46-0, Detirelix acetate 102625-70-7, Pantoprazole 102669-89-6, Saterinone 102670-59-7, Batanopride hydrochloride 102676-47-1, Fadrozole 102767-28-2, Levetiracetam 102822-56-0, Mannostatin A 102908-59-8, Binospirone 102916-21-2, Tigemonam dicholine 103060-53-3, Daptomycin 103222-11-3, Vapreotide 103255-66-9, Pazinaclone 103336-05-6, Ditekiren 103337-74-2, Letrazuril 103379-03-9, Monatepil maleate 103420-77-5, Devazepide 103475-41-8, Tepoxalin 103486-79-9, Belfosdil 103541-15-7, Clausenamide 103577-45-3, Lansoprazole 103614-76-2, Halichondrin B 103628-46-2, Sumatriptan 103745-39-7, Fasudil 103775-10-6, Moexipril 103878-84-8, Lazabemide 103890-78-4, Lacidipine 103909-75-7, 22-Oxacalcitriol 104054-27-5, Atipamezole 104153-37-9, Rilopirox 104227-87-4, Famciclovir 104340-86-5, Leminoprazole 104383-17-7, Sabeluzole 104393-00-2, Pirazmonam sodium 104454-71-9, Ipenoxazone 104456-95-3, Cisconazole 104595-79-1, Anaritide acetate 104713-75-9, Barnidipine 104719-71-3, Lorcinadol 104775-36-2, Ecabapide 104987-11-3, Tacrolimus 105102-18-9, Tibenelast sodium 105102-22-5, Mometasone 105118-12-5, Piroxantrone hydrochloride 105149-04-0, Osaterone 105182-45-4, Fluparoxan 105219-56-5, Apafant 105250-86-0, Ebiratide 105431-72-9, Linopirdine 105462-24-6, Risedronic acid 105567-83-7, Berefrine 105613-48-7, Exametazime 105615-58-5, Oxaunomycin 105687-93-2, Sumarotene 105705-89-3 105784-61-0, Temafloxacin hydrochloride 105806-65-3, Efegatran 105851-17-0, fludeoxyglucosef18 105889-45-0, Cefcapene pivoxil 105913-11-9, Plasminogen activator

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release active ingredients)

IT 105920-77-2, Camonagrel 105956-97-6, Clinafloxacin 105979-17-7, Benidipine 106243-16-7, Thioperamide 106266-06-2, Risperdal 106282-98-8, Somalapor 106400-81-1, Lometrexol 106463-17-6, Tamsulosin hydrochloride 106498-99-1, Vintoperol 106516-24-9, Sertindole 106560-14-9, Faropenem 106602-62-4, Amylin 106730-54-5, Olprinone 106861-44-3, Mivacurium chloride 107000-34-0, Zanoterone 107167-31-7, Lactivicin 107266-08-0, Carvotroline 107361-33-1, Enazadrem 107407-62-5, Nelezaprine maleate 107429-63-0, Lintopride 107703-78-6, Glemanserin 107724-20-9, Epoxymexrenone 107753-78-6, Zafirlukast

107793-72-6, Ioxilan 107868-30-4, Exemestane 107902-67-0, Tazofelone 108073-62-7, Carbazomycin C 108310-20-9, Pirodomast 108609-34-3, Lixazinone sulfate 108612-45-9, Mizolastine 108674-87-9, Sergolexole maleate 108700-03-4, Teludipine hydrochloride 108736-35-2, Lanreotide 108778-82-1, Beractant 108852-90-0, Nemorubicin 108945-35-3, Taprostene 109214-55-3, Libenzapril 109229-58-5, Englitazone 109543-76-2, Romazarit 109636-76-2, Prinomide tromethamine 109837-67-4, Cycloplatam 109889-09-0, Granisetron 110101-66-1, Tirilazad 110140-89-1, Ridogrel 110267-81-7, Amrubicin 110311-27-8, Sulofenur 110347-85-8, Selfotel 110588-56-2, Noberastine 110588-57-3, Saperconazole 110623-33-1, Suritozole 110690-43-2, Emitefur 110703-94-1, Zopolrestat 110845-89-1, Remiprostol 110871-86-8, Sparfloxacin 111011-63-3, Efonidipine 111025-46-8, Pioglitazone 111073-18-8, Nemazoline hydrochloride 111149-90-7, Lodelaben 111212-85-2, Ersofermin 111223-26-8, Ceronapril 111406-87-2, Zileuton 111490-36-9, Zeniplatin 111523-41-2, Enloplatin 111672-14-1, Rocastine hydrochloride 111686-79-4, Remacemide hydrochloride 111753-73-2, Satigrel 111786-07-3, Prinoxodan 111902-57-9, Temocapril 111974-60-8, Ritolukast 111974-69-7, Quetiapine 112018-00-5, Tebufelone 112018-01-6, Bemoradan 112192-04-8, Roxindole 112243-58-0, Gevotroline hydrochloride 112344-52-2, Flobufen 112362-50-2, Dalfopristin 112515-43-2, Topsentin 112522-64-2, Acetyldinaline 112573-73-6, Ecadotril 112733-06-9, Zenarestat 112809-51-5, Letrozole 112856-44-7, Losigamone 112859-71-9, Fluasterone 112885-41-3, Mosapride 112887-68-0, Raltitrexed 112893-26-2, Becliconazole 112922-55-1, Cericlamine 112924-45-5, Sinnabidiol 112964-97-3, Ocfentanil hydrochloride 112965-21-6, Calcipotriene 113082-98-7, Enalkiren 113102-19-5, Rifamexil 113108-86-4, Suronacrine maleate 113359-04-9, Cefozopran 113378-31-7, Semduramicin 113427-24-0, Epoetin alfa 113471-15-1 113558-15-9, baohuoside 1 113593-34-3, Flosatidil 113658-85-8, Trombodipine 113662-23-0, Gadobenic acid 113665-84-2, Clopidogrel 113775-47-6, Dexmedetomidine 113806-05-6, Olopatadine 113852-37-2, Cidofovir 113932-41-5, Tematropium methyl sulfate 113957-09-8, Cebaracetam 114030-44-3, Dexpemedolac 114084-78-5, Ibandronic acid 114118-91-1, Tirandalydigin 114285-68-6, Lentinan sulfate 114298-18-9, Zalospirone 114317-44-1, magainin 2 amide 114432-13-2, Fantofarone 114517-02-1, Fosquidone 114716-16-4, Pemedolac 114798-26-4, Losartan 114977-28-5, Docetaxel 115103-54-3, Tiagabine 115150-59-9, Antagonist G 115256-11-6, Dofetilide 115308-98-0, Tallimustine 115436-72-1, Risedronate sodium 115436-73-2, Ipazilide 115566-02-4, Bistratene A 115575-11-6, Liarozole 115743-28-7, Curdlan sulfate 115762-17-9, Ruzadolane 115956-12-2, Dolasetron 116057-75-1, Idoxifene 116078-65-0, Bidisomide 116287-14-0, Lanperisone 116290-93-8, Hatomamicin 116313-94-1, Nitecapone 116476-13-2, Semotiadil 116523-57-0 116644-53-2, Mibefradil 116649-85-5, Ramatroban 116666-63-8, Mibefradil dihydrochloride 116684-92-5, Galdansetron 116818-99-6, Isalsteine 116853-25-9, Cefluprenam 116907-13-2, Risotilide hydrochloride 117048-59-6, combretastatin A4 117086-68-7, Ricasetron 117211-03-7, Cefetecol 117268-95-8, Brifentanil hydrochloride 117467-28-4, Cefditoren pivoxil 117523-47-4, Mirfentanil 117545-11-6, Bimakalim 117581-05-2, Serazapine hydrochloride 117827-81-3, Delfaprazine 117857-45-1, Loreclezole 117946-91-5, Luzindole 117976-90-6, Rabeprazole sodium 118072-93-8, Zoledronic acid 118288-08-7, Lafutidine 118292-40-3, Tazarotene 118353-05-2, Carbovir 118395-73-6, Chloroorienticin A 118457-14-0, Nebivolol 118635-52-2, Tilnoprofen arbamel 118909-22-1, Velnacrine maleate 119006-77-8, Flutrimazole 119129-70-3, Ananain 119169-78-7, Epristeride 119257-34-0, Besipirdine 119302-91-9, Rocuronium bromide 119413-54-6, Topotecan hydrochloride 119413-55-7, Elgodipine 119422-08-1 119431-25-3, Eliprodil 119509-26-1, Atpenin B 119514-66-8, Lifarizine 119625-78-4, Terlakiren 119683-68-0, Ferumoxides 119693-74-2, Somenopor 119758-39-3, Maduramicin 119813-10-4, Carzelesin 119817-90-2, Dexloxiglumide 119905-05-4, Delequamine 119914-60-2, Grepafloxacin 120066-54-8, Gadoteridol 120128-20-3, RG 12525 120138-50-3, Quinupristin 120210-48-2, Tenidap 120287-85-6, Cetrorelix 120360-10-3, Batelapine maleate 120373-24-2, Isopropyl unoprostone 120410-24-4, Biapenem 120443-16-5, Verlukast 120444-71-5, Deramciclane 120500-15-4, Leinamycin 120511-73-1, Anastrozole 120551-59-9,

Crilvastatin 120635-25-8, Mofegiline hydrochloride 120635-74-7, Cilansetron 120656-93-1, Trefentanil hydrochloride 120685-11-2, Benzoylstaurosporine 120788-07-0, Sulopenem 120824-08-0, Linotroban 120993-53-5, Desirudin 121181-53-1, Filgrastim 121249-14-7, Corticorelin ovine triflutate 121263-19-2, Calphostin C 121281-41-2, technetium Tc 99 m bicisate 121288-39-9, Loxoribine 121547-04-4, Mirimostim 121650-80-4, Pancopride 121679-13-8, Naratriptan 121749-39-1 121808-62-6, Pidotimod 121929-46-2, Zoniclezole hydrochloride 122312-54-3, Epoetin beta 122341-38-2, Temoporfin 122431-96-3 122535-63-1, α-Citreamicin 122566-70-5, Maniwamycin A 122575-28-4, Naglivan 122647-32-9, Ibutilide fumarate 122841-10-5, Cefoselis 122898-63-9, Phenazinomycin 122898-67-3, Itopride 122946-43-4, Telmesteine 122955-18-4, Sibopirdine 123039-93-0, Dihydrexidine 123040-69-7, Azasetron 123072-45-7, Aprosulate sodium 123122-54-3, Candoxatrilat 123122-55-4, Candoxatril 123258-84-4, Itasetron 123308-22-5, Sezolamide 123407-36-3, Arteflene 123447-62-1, Prulifloxacin 123482-22-4, Zatosetron 123482-23-5, Zatosetron maleate 123524-52-7, Azelnidipine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release active ingredients)

IT 123618-00-8, Fedotozine 123774-72-1, Sargramostim 123830-79-5, Teloxantrone hydrochloride 123948-87-8, Topotecan 124012-42-6, Galocitabine 124423-84-3, Panadiplon 124436-59-5, Pirodavir 124439-07-2, Enadoline hydrochloride 124508-99-2, Sulfinosine 124770-85-0, Cyclobut A 124784-31-2, Erbulozole 124832-26-4, Valaciclovir 124858-35-1, Nadifloxacin 124904-93-4, Ganirelix 124916-54-7, Celikalim 125251-66-3, Arbutamine hydrochloride 125279-79-0, Ersentilide 125472-02-8, Mivazerol 125533-88-2, Mofarotene 125722-16-9, Enofelast 125926-17-2, Sarpogrelate 126062-18-8, Cyclobut G 126100-97-8, Dimiracetam 126297-39-0, lissoclinamide 7 126443-96-7, Napavin 126544-47-6, Ciclesonide 126595-07-1, Propagermanium 126825-36-3, Bertosamil 127000-20-8, Gadobenate dimeglumine 127045-41-4, Pazufloxacin 127294-70-6, Balofloxacin 127304-28-3, Linarotene 127502-06-1, Tetrofosmin 127685-30-7, Seproxetine hydrochloride 127757-45-3, cyclic HPMPC 127757-91-9, Regramostim 127759-89-1, Lobucavir 127779-20-8, Saquinavir 127785-64-2, Aureobasidin A 127943-53-7, Discodermolide 128075-79-6, Lufironil 128270-60-0, Bivalirudin 128312-51-6, Cinalukast 128470-17-7, Sprodiamide 128505-88-4, Naphterpin 128768-09-2, Placetin A 129029-23-8, Ocaperidone 129038-42-2, Echistatin 129242-14-4 129260-79-3, Loteprednol 129277-10-7, Asperfuran 129369-64-8, Irtemazole 129388-07-4, Levdobutamine lactobionate 129497-78-5, Verteporfin 129564-92-7, Azatoxin 129618-40-2, Nevirapine 129655-21-6, Bizelesin 129722-12-9, Aripiprazole 129731-10-8, Vorozole 129938-20-1, Dapoxetine hydrochloride 129981-36-8, Sampatrilat 130123-69-2, Faeriefungin 130167-69-0, Pegaspargase 130209-82-4, Latanoprost 130364-39-5, Rubiginone B1 130370-60-4, Batimastat 130610-93-4, Niravoline 130641-36-0, Picumeterol 130641-38-2, Bindarit 130800-90-7, Sipatrigine 130804-35-2, Lecimibide 130929-57-6, Entacapone 131069-91-5, Gadoversetamide 131081-40-8, Silteplase 131094-16-1, Trafermin 131129-98-1, Mipragoside 131190-63-1, Saintopin 131410-48-5, Gadodiamide 131707-23-8, Arbidol 131741-08-7, Simendan 131956-33-7, Depsidomycin 131986-45-3, Xanomeline 132036-88-5, Ramosetron 132073-72-4, Tetrazomine 132100-55-1, Dalvastatin 132199-13-4, Carsatrin succinate 132203-70-4, Cilnidipine 132210-43-6, Cipamfylline 132236-18-1, Zifrosilone 132373-81-0, Vamicamide 132449-46-8, Lesopitron 132539-06-1, Olanzapine 132539-07-2, Remifentanil hydrochloride 132722-74-8, Pirsidomine 133040-01-4, Eprosartan 133099-04-4, Darifenacin 133247-60-6, Triflavin 133267-20-6, Artilide fumarate 133352-26-8, Cyclothiazomycin 133352-27-9, Lydicamycin 133432-71-0, Peldesine 133454-47-4, Iloperidone 133692-55-4, Seprilose 133718-29-3, Revizinone 134088-74-7, Nartograstim 134143-28-5, Glaspimod 134208-18-7, Mazapertine succinate 134308-13-7, Tolcapone 134352-59-3, Symakalim 134377-69-8, Safironil 134381-30-9, Conagenin 134499-06-2, Silipide 134523-03-8, Atorvastatin calcium 134523-84-5 134564-82-2, Befloxatone 134633-29-7, Tecogalan sodium 134678-17-4, Lamivudine 134861-62-4,

Dioxamycin 135003-30-4, Apadoline 135038-56-1, Glycopril
135038-57-2, Fasidotril 135202-79-8, Ilonidap 135247-46-0, Tylogenin
135257-45-3, crambescidin 816 135381-77-0, Flezelastine 135383-02-7,
Stipiamide 135459-90-4, Ranelic acid 135558-11-1, Lobaplatin
135819-69-1 135968-09-1, Lenograstim 136279-32-8, Teceleukin
136310-93-5, Tiotropium bromide 136381-85-6, Lintitript 136668-42-3,
Quiflapon 136777-43-0, Carvotroline hydrochloride 136816-75-6,
Atevirdine 136949-58-1, Iobitridol 137018-54-3, Okicenone
137023-81-5, Pannorin 137099-09-3, Turosteride 137109-71-8, Balazipone
137159-92-3, Aptiganel 137219-37-5, Dehydrodidemnin B 137234-62-9,
Voriconazole 137500-42-6, Darsidomine 137571-30-3 137647-92-8,
Axinastatin 1 137862-53-4, Valsartan 137893-48-2, Michellamine B
138071-82-6, Gadobutrol 138402-11-6, Irbesartan 138614-30-9, Icatibant
acetate 138660-96-5, Sevirumab 138705-61-0 138708-32-4, Ferpifosate
sodium 138742-43-5, Zankiren 138955-27-8 139110-80-8, Zanamivir
139133-26-9, Lexipafant 139225-22-2, Panamesine 139264-17-8,
Zolmitriptan 139403-31-9, Pimilprost 139481-59-7, Candesartan
139501-91-0, Hatomarubigin B 139501-92-1, Hatomarubigin C 139501-93-2,
Hatomarubigin D 139562-86-0, Hatomarubigin A 139664-68-9
139886-32-1, Milameline 140703-49-7, Meterelin 140703-51-1, Examorelin
140709-07-5 140932-79-2, Balhimycin 140945-32-0, Mapinastine
141205-31-4, Microcolin A 141410-98-2, Edobacomab 141505-33-1,
Levosimendan 141660-63-1, Iofratol 142298-00-8, Emoctakin
142439-86-9, Halomon 142632-32-4, Calanolide A 142864-19-5, Enlimomab
142880-36-2, Ilomastat 142985-55-5 143090-92-0, Anakinra
143248-63-9, Sinitrodil 143257-97-0, Sameridine 143257-98-1,
Lerisetron 143322-58-1, Eletriptan 143413-62-1, Betaclamycin B
143443-90-7, Ifetroban 143484-82-6, Azalanstat dihydrochloride
143486-90-2, Lurosetron mesylate 144285-84-7, ecteinascidin 722
144412-49-7, Lamifiban 144494-65-5, Tirofiban 144665-07-6, Lubeluzole
144701-48-4, Telmisartan 144849-63-8, Bisnafide 144916-42-7, Sonermin
145071-44-9, Itameline 145202-66-0, Rizatriptan benzoate 145216-43-9,
Forasartan 145414-12-6, Lirexapride 145599-86-6, Cerivastatin
145686-15-3, Azadirachtin E 145733-36-4, Tasosartan 146426-40-6,
Flavopiridol 146623-69-0, Saprisartan 146929-33-1, Cyclazosin
146939-27-7, Ziprasidone 147059-72-1, Trovafloxacin 147214-63-9,
Cyclothialidine 147221-93-0, Delavirdine mesylate 147249-33-0,
Aspalatone 147362-57-0, Loviride 147432-77-7, Ontazolast
147536-97-8, Bosentan 147541-45-5, Cilobradine 148317-76-4, Oracin
148504-51-2, Ripisartan 148611-75-0, Mirisetron maleate 148717-58-2,
Palauamine 148717-90-2, Squalamine 148937-32-0, Echicetin
149204-42-2, Kahalalide F 149260-80-0, Mycaperoxide B 149355-77-1,
Lamellarin-N triacetate 149488-17-5, Trovirdine 149633-91-0,
Leptolstatin 149649-22-9, Nafadotride 149715-96-8, spongistatin 1
149820-74-6, Xemilofiban 149845-07-8, Tiludronate disodium
149882-10-0, Lurtotecan 149904-87-0, Darglitazone sodium 149908-53-2,
Azimilide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release
active ingredients)

IT 150332-35-7, Pamaqueside 150378-17-9, Indinavir 150829-93-9, Nisamycin
150915-41-6, Perospirone 150977-36-9, Bromelain 151271-08-8,
Imidazenil 151272-78-5, Antarelix 151319-34-5, Zaleplon 151581-23-6,
Apaxifylline 151767-02-1, Montelukast sodium 152923-56-3, Dacliximab
152981-31-2, Inolimomab 153101-26-9, Regavirumab 153205-46-0,
Asimadoline 153438-49-4, Dapitant 153723-34-3, Axinastatin 2
153723-35-4, Axinastatin 3 153858-68-5, Contortrostatin 154039-60-8,
Marimastat 154212-56-3, Cosalane 154248-96-1, Iroplact 154277-21-1,
Cypemycin 154361-50-9, Capecitabine 154397-77-0, Napsagatran
154612-39-2, Palinavir 155213-67-5, Ritonavir 155233-30-0, Curacin A
155319-91-8, Mangafodipir 155415-08-0, Inogatran 155660-91-6,
Bistramide D 155660-92-7, Bistramide k 155773-56-1, Ferristene
155773-57-2, Pegorgotein 156039-69-9, Mixanpril 156250-43-0, Manumycin
E 156317-47-4, Manumycin F 156586-89-9, Edrecolomab 156679-34-4,
Lenercept 156712-35-5, Galdansetron hydrochloride 156769-21-0,
Sanfetrinem 156790-85-1, Variolin B 157078-48-3, Isohomohalichondrin B
157207-83-5, bioxalomycin α-2 157857-21-1, Maspin 158792-24-6,
Collismycin A 158792-25-7, Collismycin B 159445-63-3, Nateplase
159519-65-0, Pentafuside 161009-41-2 161600-01-7, MCC-555

162341-15-3, Darlucin A 163663-18-1, Protegrin 164325-97-7, Veroxanon 165101-51-9, Becaplermin 168482-36-8, cryptophycin 8 169494-85-3, Leptin 170861-63-9, JTT-501 171544-35-7, Ferumoxsil 172647-53-9, DRF-2189 172793-30-5 173046-02-1, Thiocoraline 173940-41-5, Tapgen 174305-65-8, Breflate 177402-92-5, Curiosin 178303-21-4, Ferucarbotran 178806-87-6, Eudragit RSPO 188364-40-1, CARN 700 189339-64-8 191034-25-0, L 168049 193012-35-0, FK614 196808-24-9, GW 1929 200139-38-4, Suradista 200631-89-6, CRE-16336 202532-75-0 207309-33-9, Motilide 209808-51-5, L 805645 212894-59-2, Pentrozole 213252-19-8, KRP-297 213411-84-8, BM-152054 213594-60-6, Balsalazide disodium 222834-30-2, Ragaglitazar) 245075-84-7, LR 90 246252-06-2, Gadolinium texaphyrin 250601-04-8, TAK559 251565-85-2 251572-86-8 308804-09-3, GW 9820 321942-74-9, Phensuccinal 324740-00-3, Vitaxin 331741-94-7, BMS298585 345631-66-5, Eveminomycin 385390-37-4, Pobilukast edamine 441772-39-0, Isobengazole 441772-43-6, Nagrestip 441772-66-3, Vinxaltine 441774-07-8, Spicamycin D 441774-77-2, Solverol 514172-76-0 516482-86-3, Sermorelin acetate 524675-01-2, CS 011 679809-58-6, Enoxaparin sodium 753015-01-9, Enterostatin 808103-38-0, Cepacidine 812697-78-2, CLX 0940 869997-64-8, R 483 873298-28-3, NIP 223 875140-52-6 875140-53-7 875338-33-3 875338-35-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release active ingredients)

IT 60529-76-2, Thymopoietin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(receptor agonists; novel dosage form comprising modified-release and immediate-release active ingredients)

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ACCESSION NUMBER: 2006023873 EMBASE
TITLE: Recent insights into androgen action on the anatomical and physiological substrate of penile erection.
AUTHOR: Gooren L.J.G.; Saad F.
CORPORATE SOURCE: Prof. L.J.G. Gooren, Department of Endocrinology, Andrology Section, Vrije Universiteit Medical Center, P.O. Box 7057, 1007 MB Amsterdam, Netherlands. ljg.gooren@vumc.nl
SOURCE: Asian Journal of Andrology, (2006) Vol. 8, No. 1, pp. 3-9.
.
Refs: 44
ISSN: 1008-682X CODEN: ASJAF8
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
028 Urology and Nephrology
030 Pharmacology
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20060126
Last Updated on STN: 20060126

AB Erectile response is centrally and peripherally regulated by androgens. The original insights into the mechanisms of action of androgens were that androgens particularly exert effects on libido and that erections in response to erotic stimuli were relatively androgen-independent. It was shown that sexual functions in men required androgen levels at the low end of reference values of testosterone. So it seemed that testosterone was not useful treatment for men with erectile difficulties, particularly following the advent of the phosphodiesterase type 5 (PDE5) inhibitors. However, approximately 50% of those treated with PDE5 inhibitors discontinue their treatment. A number of recent developments shed new light on testosterone treatment of erectile dysfunction (ED) in **aging** men. (1) A recent insight is that, in contrast to younger men, elderly men might require higher levels of testosterone for normal sexual functioning. (2) Several studies have indicated that PDE5 inhibitors are not always sufficient to restore erectile potency in men, and that testosterone improves the therapeutical response to PDE5

inhibitors considerably. (3) There is growing insight that testosterone has profound effects on tissues of the penis involved in the mechanism of erection and that testosterone deficiency impairs the anatomical and physiological substrate of erectile capacity, reversible upon androgen replacement. The synthesis of PDE5 is upregulated by androgens, and the arterial inflow into the penis is improved by giving androgen. The above invites a re-examination of the merits of giving testosterone to **aging** men with ED. The beneficial effects of PDE5 inhibitors may only be optimally expressed in a eugonadal enviromnent. 

L23 ANSWER 3 OF 160 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:259887 CAPLUS
DOCUMENT NUMBER: 142:336518
TITLE: Preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivatives as androgen receptor modulators
INVENTOR(S): Meissner, Robert S.; Mitchell, Helen J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005025579 | A1 | 20050324 | WO 2004-US28641 | 20040902 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-501664P P 20030910
OTHER SOURCE(S): MARPAT 142:336518
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention discloses preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs., such as I [dashed bond = single bond, double bond; X = H, halo; Y, Z = H, alkyl, halo; Y and Z, together with the carbon atom to which they are attached = cyclopropyl; n = 0-3; U, V, W, D = CH, N, provided that at least U, V, W, and D = CH; R1 = H, CF3, carbonyl(alkyl), OH, alkoxy, halo, alkyl, CH2OH, alkylamino; R2 = halo, carbonyl(alkyl), carbonyl(alkenyl), carbonyl(alkynyl), alkenylamino, heterocyclic, etc.], for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, 4-azaandrost-1-ene derivative II was reacted with 2,3-diaminopyridine in presence of silver triflate to give 17β-carboxamide derivative III, which, on heating with polyphosphoric acid, afforded 17β-imidazopyridinyl-3-oxo-4-aza-5α-androst-1-ene derivative IV. I are therefore useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, **aging** skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia,

hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, **HIV**-wasting, prostate cancer, benign prostatic hyperplasia (BPH), abdominal adiposity, metabolic syndrome, type II diabetes, cancer **cachexia**, Alzheimer's disease, muscular dystrophies, cognitive decline, sexual dysfunction, sleep apnea, depression, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

IT Bone morphogenetic proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(2; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Bone morphogenetic proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(3; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Bone morphogenetic proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(5; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Bone morphogenetic proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(6; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Bone morphogenetic proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(7; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Animal cell line
(Hep G2; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Insulin-like growth factor-binding proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IGFBP-3; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT **AIDS** (disease)
(Wasting; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Obesity
(abdominal; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(an inhibitor of BMP antagonism, bone strengthening agents as adjuvant therapeutics; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Anemia (disease)
(aplastic; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Prostate gland, disease
(benign hyperplasia; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Hyperplasia
(benign prostatic; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Bone minerals
(bone mineral d. (BMD); preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Estrogens
Prostaglandins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(bone strengthening agents as adjuvant therapeutics; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(calcium, antagonist; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT **Cachexia**
(cancerous; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Drug delivery systems
(capsules; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Mental and behavioral disorders
(depression; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Bone, disease
(fracture; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hyperlipidemia; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Testis, disease
(hypogonadism; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Drug delivery systems
(injections, s.c.; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Disease, animal
(metabolic syndrome X; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Estrogen receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulator; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Drug delivery systems
(nasal sprays; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Diabetes mellitus
(non-insulin-dependent; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Heterocyclization
(of 17β-carboxamide in preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Bone, disease
(osteopenia; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Surgery
(plastic; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Menopause
(postmenopause, postmenpausal symptoms in women; preparation of

17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Alzheimer's disease
Atherosclerosis
Autoimmune disease
Cognitive disorders
Hematopoietic disorders
Human
Hypercholesterolemia
Joint, anatomical
Muscular dystrophy
Osteoarthritis
Osteoporosis
Periodontium, disease
Prostate gland, neoplasm
Rheumatoid arthritis
Sexual disorders
Sleep apnea
(preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Androgen receptors
Prostacyclin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Polyphosphoric acids
RL: RGT (Reagent); RACT (Reactant or reagent)
(preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Arthritis
(repair; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Androgens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(replacement therapy; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Fluorides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(salts as bone strengthening agents as adjuvant therapeutics; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Muscle
(sarcopenia; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type EP1; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type EP2; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type EP4; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type FP; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Collagens, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(type I, C-telopeptide, as bone turnover marker; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Collagens, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(urinary N-telopeptide cross-links to type I collagen (NTX), DXA and DPD as bone turnover marker; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(αvβ3, antagonist; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Transforming growth factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β-; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(γ, an activator; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT 127464-60-2, Vascular endothelial growth factor
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(an antagonist of VEGF binding to osteoclast receptors; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT 50-28-2, 17β-Estradiol, biological studies 53-16-7, Estrone, biological studies 57-83-0, Progestin, biological studies 64-96-0, U-11,555A 67-96-9, Dihydrotachysterol 67-98-1, Mer-25 68-22-4, Norethindrone 71-58-9, Medroxyprogesterone acetate 471-34-1, Calcium carbonate, biological studies 911-45-5, **Clomiphene** 1406-16-2, Vitamin D 1845-11-0, Nafoxidene 2809-21-4, Etidronate 4717-38-8, 17β-Ethynyl estradiol 5863-35-4, CI-628 7681-49-4, Sodium fluoride, biological studies 7693-13-2, Calcium citrate 9002-64-6, Parathyroid hormone 9004-10-8D, Insulin, insulin-like growth factor 9007-12-9, Calcitonin 10540-29-1, Tamoxifen 10596-23-3, Clodronate 12001-79-5, Vitamin K 12629-01-5, Human growth hormone 15690-55-8, Zuclomiphene 15690-57-0, **Enclomiphene** 19356-17-3, 25-Hydroxy-vitamin D3 20859-36-3, Monosodium fluorophosphate 32222-06-3, 1α,25-Dihydroxy-vitamin D3 40391-99-9, Pamidronate 41294-56-8, 1α-Hydroxy-vitamin D3 47931-85-1, Calcitonin, salmon 54573-75-0, 1α-Hydroxy-vitamin D2 56287-31-1, CI-680 57333-95-6, 1α,24(S)-Dihydroxy-vitamin D3 57333-96-7, 1α,24(R)-Dihydroxy-vitamin D3 66376-36-1, Alendronate 67763-96-6, Insulin-like growth factor I 67763-97-7, Insulin-like growth factor II 68893-82-3, Human parathyroid hormone (1-84) 75330-75-5, Lovastatin 75755-07-6, Piridronate 78994-23-7, Levormeloxifene 79778-41-9, Neridronate 79902-63-9, Simvastatin 81093-37-0, Pravastatin 82413-20-5, Droloxifene 83805-11-2 84449-90-1, Raloxifene 89778-26-7, Toremifen 89987-06-4, Tiludronate 93957-54-1, Fluvastatin 103909-75-7, 22-Oxacalcitriol 104121-92-8, ED71 105462-24-6, Risedronate 106096-92-8, Acidic fibroblast growth factor 106096-93-9, Basic fibroblast growth factor 112965-21-6, Calcipotriol 114084-78-5, Ibandronate 116057-75-1, Idoxifene 118072-93-8, Zoledronate 118694-43-2, Ro 23-7553 121009-77-6 121268-17-5, Alendronate monosodium trihydrate 121368-58-9, Olpadronate 130447-37-9, 19-Nor-1α,25-Dihydroxy-vitamin D3 131875-08-6, KH1060 134404-52-7, EB1089 134523-00-5, Atorvastatin 134523-84-5, 20-epi-1α,25-Dihydroxy-vitamin D3 138330-18-4, Incadronate 141750-63-2, Nisvastatin 145599-86-6, Cerivastatin 147511-69-1, Pitavastatin 180064-38-4, Minodronate 180916-16-9, Lasofoxifene 182133-25-1, Arzoxifene 182167-02-8, EM-652 182167-03-9, EM-800 198481-33-3, TSE-424 205944-50-9, Osteoprotegrin 260055-05-8,

Alendronate monosodium monohydrate 287714-41-4, Rosuvastatin 304853-26-7, Growth hormone secretagogue 372092-80-3D, Protein Kinase, p38 protein Kinase inhibitor 797050-81-8, U-100A
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bone strengthening agents as adjuvant therapeutics; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT 7440-70-2, Calcium, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dietary supplement; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT 1553-55-5, HMG-CoA 52232-67-4, Human parathyroid hormone (1-34) 94716-09-3, Cathepsin K
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor as adjuvant therapeutics; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT 9000-83-3, ATPase
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(osteoclast vacuolar ATPase inhibitor as adjuvant therapeutics; preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT 9002-64-6D, Parathyroid hormone, analog 193830-08-9, Growth differentiation factor 5
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT 848392-90-5P 848392-94-9P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT 848392-91-6P 848392-92-7P 848392-93-8P 848392-95-0P 848392-96-1P 848392-97-2P 848392-98-3P 848392-99-4P 848393-00-0P 848393-01-1P 848393-02-2P 848393-03-3P 848393-04-4P 848393-05-5P 848393-06-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT 15477-76-6D, Phosphonate, bisphosphonate derivs. 35212-22-7, Ipriflavone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT 54-96-6, 3,4-Pyridinediamine 74-88-4, Methyl iodide, reactions 75-36-5, Acetyl chloride 95-83-0 102-51-2 368-71-8 452-58-4, 2,3-Diaminopyridine 496-72-0 2687-25-4 3171-45-7 5348-42-5 13754-19-3, 4,5-Pyrimidinediamine 17626-40-3 86283-81-0 103335-47-3 133745-75-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT 606101-77-3P 606101-78-4P 848393-07-7P 848393-08-8P 848393-09-9P 848393-10-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

IT 2923-28-6, Silver triflate
RL: RGT (Reagent); RACT (Reactant or reagent)
(preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs. as androgen receptor modulators and their therapeutic uses)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 4 OF 160 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:259881 CAPLUS
DOCUMENT NUMBER: 142:336517
TITLE: Preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivatives for their use as modulators of the androgen receptor in a tissue selective manner
INVENTOR(S): Kaufman, Mildred L.; Meissner, Robert S.; Mitchell, Helen J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005025572 | A1 | 20050324 | WO 2004-US28655 | 20040902 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-501789P P 20030910
OTHER SOURCE(S): MARPAT 142:336517
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB 17-Heterocyclic-4-aza-5α-androst-1-en-3-one derivs., such as I [dashed bond = single bond, double bond; X = H, halo; Y, Z = H, alkyl, halo; Y and Z, together with the carbon atom to which they are attached = cyclopropyl; n = 0-3; U, V, W, D = CH, N, S, O; R1 = H, CF3, carbonyl(alkyl), OH, alkoxy, halo, alkyl, CH2OH, alkylamino; R2 = halo, carbonyl(alkyl), carbonyl(alkenyl), carbonyl(alkynyl), alkenylamino, heterocyclic, etc.], were prepared for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, II (R = OH) was treated with Et3N, and iso-Bu chloroformate, followed by reaction with N,O-dimethylhydroxylamine hydrochloride to give II [R = N(Me)OMe (III)]. III was converted to 4-aza-5α-androst-1-en-3,20-dione derivative II (R = Me), and then to bromide II [R = CH2Br (IV)], which was treated with N-butyl-thiourea to afford V. The prepared compds. are useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, **aging** skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, **HIV**-wasting, prostate cancer, benign prostatic hyperplasia (BPH), abdominal adiposity, metabolic syndrome, type II diabetes, cancer **cachexia**, Alzheimer's disease, muscular dystrophies, cognitive decline, sexual dysfunction, sleep apnea, depression, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(2, bone strengthening agents as adjuvant therapeutics; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(3, bone strengthening agents as adjuvant therapeutics; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(5, bone strengthening agents as adjuvant therapeutics; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(6, bone strengthening agents as adjuvant therapeutics; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(7, bone strengthening agents as adjuvant therapeutics; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Animal cell line
(Hep G2; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Insulin-like growth factor-binding proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IGFBP-3; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Obesity
(abdominal; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Skin, disease
(**aging**; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Peroxisome proliferators
(an activator of peroxisome proliferator-activated receptor γ; preparation of 17-heterocyclic-4-aza-5-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Anemia (disease)
(aplastic; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Prostate gland, disease
(benign hyperplasia; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Hyperplasia
(benign prostatic; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bone strengthening agents as adjuvant therapeutics; preparation of 17-heterocyclic-4-aza-5-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(calcium, antagonist as adjuvant therapeutics; preparation of 17-heterocyclic-4-aza-5-androst-1-en-3-one derivs. as androgen receptor

modulators and their therapeutic uses)

IT **Cachexia**
(cancerous; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Mental and behavioral disorders
(depression; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Prostaglandins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(derivs. as adjuvant therapeutics; preparation of 17-heterocyclic-4-aza-5-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Salts, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fluoride salts as adjuvant therapeutics; preparation of 17-heterocyclic-4-aza-5-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Bone, disease
(fracture; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hyperlipidemia; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Testis, disease
(hypogonadism; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Arthritis
(inflammatory; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Drug delivery systems
(injections, s.c.; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Disease, animal
(metabolic syndrome X; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Estrogen receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulator; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Drug delivery systems
(nasal sprays; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Diabetes mellitus
(non-insulin-dependent; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Estrogens
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(or an estrogen derivative, bone strengthening agents as adjuvant therapeutics; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Bone, disease
(osteopenia; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Surgery
(plastic, bone damage following bone reconstructive surgery; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Menopause
(postmenopause, postmenopausal symptoms in women; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Alzheimer's disease
Atherosclerosis
Autoimmune disease
Cognitive disorders
Hematopoietic disorders
Human
Hypercholesterolemia
Muscular dystrophy
Osteoarthritis
Osteoporosis
Periodontium, disease
Prostate gland, neoplasm
Rheumatoid arthritis
Sexual disorders
Sleep apnea
(preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Antiestrogens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Polyphosphoric acids
RL: RGT (Reagent); RACT (Reactant or reagent)
(preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Joint, anatomical
(repair; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Androgens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(replacement therapy; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Muscle
(sarcopenia; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type EP1; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type EP2; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type EP4; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type FP; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Collagens, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type I, C-telopeptide, as bone turnover marker; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Collagens, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type I, N-telopeptide, urinary N-telopeptide cross-links to type I collagen (NTX), DXA and DPD as bone turnover marker; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT **AIDS** (disease)
(wasting; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Integrins

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(αvβ3, receptor antagonist; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT Transforming growth factors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β-, bone strengthening agents as adjuvant therapeutics; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT 127464-60-2, Vascular endothelial growth factor
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(an antagonist of VEGF binding to osteoclast receptors; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT 9004-10-8D, Insulin, like growth factor 12629-01-5, Human Growth hormone 52232-67-4, Human parathyroid hormone 1-34 68893-82-3, Human parathyroid hormone 1-84 205944-50-9, Osteoprotegrin 304853-26-7, Growth hormone secretagogue
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bone strengthening agents as adjuvant therapeutics; preparation of 17-heterocyclic-4-aza-5-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT 50-28-2, 17β-Estradiol, biological studies 53-16-7, Estrone, biological studies 57-83-0, Progestin, biological studies 64-96-0 67-96-9, Dihydrotachysterol 67-98-1, Mer-25 68-22-4, Norethindrone 71-58-9, Medroxyprogesterone acetate 471-34-1, Calcium carbonate, biological studies 911-45-5, **Clomiphene** 1845-11-0, Nafoxidene 2809-21-4, Etidronate 4717-38-8, 17β-Ethynyl estradiol 5863-35-4, CI-628 7681-49-4, Sodium fluoride, biological studies 7693-13-2, Calcium citrate 9002-64-6, Parathyroid hormone 9007-12-9, Calcitonin 10540-29-1, Tamoxifen 10596-23-3, Clodronate 15690-55-8, Zuclomiphene 15690-57-0, **Enclomiphene** 19356-17-3, 25-Hydroxy-vitamin D3 20859-36-3, Monosodium fluorophosphate 32222-06-3, 1α,25-Dihydroxy-vitamin D3 35212-22-7, Ipriflavone 40391-99-9, Pamidronate 41294-56-8, 1α-Hydroxy-vitamin D3 54573-75-0, 1α-Hydroxy-vitamin D2 56287-31-1, CI-680 57333-95-6, 1α,24(S)-Dihydroxy-vitamin D3 57333-96-7, 1α,24(R)-Dihydroxy-vitamin D3 66376-36-1, Alendronate 67763-96-6, Insulin-like growth factor I 67763-97-7, Insulin-like growth factor II 75330-75-5, Lovastatin 75755-07-6, Piridronate 78994-23-7, Levormeloxifene 79778-41-9, Neridronate 79902-63-9, Simvastatin 81093-37-0, Pravastatin 82413-20-5, Droloxifene 83805-11-2 84449-90-1, Raloxifene 89778-26-7, Toremifen 89987-06-4, Tiludronate 93957-54-1, Fluvastatin 103909-75-7, 22-Oxacalcitriol 104121-92-8, ED71 105462-24-6, Risedronate 112965-21-6, Calcipotriol 114084-78-5, Ibandronate 116057-75-1, Idoxifene 118072-93-8, Zoledronate 118694-43-2, Ro 23-7553 121009-77-6 121268-17-5, Alendronate monosodium trihydrate 121368-58-9, Olpadronate 130447-37-9, 19-Nor-1α,25-Dihydroxy-vitamin D3 131875-08-6, KH1060 134404-52-7, EB1089 134523-00-5, Atorvastatin 134523-84-5, 20-epi-1α,25-Dihydroxy-vitamin D3 138330-18-4, InCadronate 141750-63-2, Nisvastatin 145599-86-6, Cerivastatin 147511-69-1, Pitavastatin 180064-38-4, Minodronate 180916-16-9, Lasofoxifene 182133-25-1, Arzoxifene 182167-02-8, EM-652 182167-03-9, EM-800 193830-08-9, GDF5 198481-33-3, TSE-424 260055-05-8, Alendronate monosodium monohydrate 287714-41-4, Rosuvastatin 797050-81-8, U-100A
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bone strengthening agents as adjuvant therapeutics; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT 1406-16-2, Vitamin D 12001-79-5, Vitamin K
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(derivs. as adjuvant therapeutics; preparation of 17-heterocyclic-4-aza-5-

androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT 7440-70-2, Calcium, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dietary supplement as adjuvant therapeutics; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT 1553-55-5, HMG-CoA 9028-35-7, HMG-CoA reductase 94716-09-3, Cathepsin K
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor as adjuvant therapeutics; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT 9000-83-3, ATPase
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(osteoclast vacuolar ATPase inhibitor as adjuvant therapeutics; preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT 165245-96-5, p38 Kinase
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(p38 protein kinase inhibitor as adjuvant therapeutics; preparation of 17-heterocyclic-4-aza-5-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT 3098-03-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 17-heterocyclic-4-aza-5-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT 7440-05-3, Palladium, uses
RL: CAT (Catalyst use); USES (Uses)
(preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT 848353-58-2P 848353-79-7P 848353-80-0P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT 848353-29-7P 848353-30-0P 848353-31-1P 848353-32-2P 848353-33-3P
848353-34-4P 848353-35-5P 848353-36-6P 848353-37-7P 848353-38-8P
848353-39-9P 848353-40-2P 848353-41-3P 848353-42-4P 848353-43-5P
848353-44-6P 848353-45-7P 848353-46-8P 848353-47-9P 848353-48-0P
848353-49-1P 848353-50-4P 848353-51-5P 848353-52-6P 848353-53-7P
848353-54-8P 848353-55-9P 848353-56-0P 848353-57-1P 848353-59-3P
848353-60-6P 848353-61-7P 848353-62-8P 848353-63-9P 848353-64-0P
848353-65-1P 848353-66-2P 848353-67-3P 848353-68-4P 848353-69-5P
848353-70-8P 848353-71-9P 848353-72-0P 848353-73-1P 848353-74-2P
848353-75-3P 848353-76-4P 848353-77-5P 848353-78-6P 848353-81-1P
848353-82-2P 848353-83-3P 848353-84-4P 848353-86-6P 848353-87-7P
848353-88-8P 848353-89-9P 848353-90-2P 848353-91-3P 848353-92-4P
848353-93-5P 848353-94-6P 848353-95-7P 848353-96-8P 848353-97-9P
848353-98-0P 848353-99-1P 848354-00-7P 848354-01-8P 848354-02-9P
848354-03-0P 848354-04-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT 106096-92-8, Acidic fibroblast growth factor 106096-93-9, Basic fibroblast growth factor
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT 57-13-6, Urea, reactions 62-55-5, Ethanethioamide 62-56-6, Thiourea, reactions 75-16-1, Methylmagnesium bromide 75-36-5, Acetyl chloride

79-17-4, Aminoguanidine 98-88-4, Benzoyl chloride 103-85-5 108-23-6
108-91-8, Cyclohexanamine, reactions 109-57-9 109-81-9 110-85-0,
Piperazine, reactions 110-91-8, Morpholine, reactions 124-40-3,
reactions 124-42-5, Acetamidine hydrochloride 124-63-0,
Methanesulfonyl chloride 459-05-2 462-08-8, 3-Pyridinamine 462-27-1
504-29-0, 2-Pyridinamine 527-69-5, 2-Furancarbonyl chloride 530-62-1,
N,N-Carbonyldiimidazole 541-41-3 598-50-5 598-52-7 598-94-7
618-39-3, Benzenecarboximidamide 621-83-0 656-32-6 765-30-0,
Cyclopropanamine 927-67-3 1516-32-1 1719-76-2 2114-02-5
3218-02-8, Cyclohexanemethanamine 3460-55-7 4104-75-0 4621-66-3,
3-Pyridinecarbothioamide 5055-72-1 5271-67-0, 2-Thiophenecarbonyl
chloride 5699-40-1 6638-79-5, N,O-Dimethylhydroxylamine hydrochloride
7204-48-0 7357-70-2 7664-41-7, Ammonia, reactions 7726-95-6,
Bromine, reactions 10400-19-8, 3-Pyridinecarbonyl chloride 13281-03-3
14254-57-0, 4-Pyridinecarbonyl chloride 14294-11-2 15717-17-6
16982-21-1 19847-10-0, Pyrazinecarbonyl chloride 21071-27-2
22906-75-8 24608-52-4 29745-44-6, 2-Pyridinecarbonyl chloride
30162-37-9 31437-20-4 41507-35-1, 3-Thiophenecarbonyl chloride
41716-12-5 58326-38-8 62366-45-4 66892-33-9 84545-31-3
94813-61-3 96692-02-3 102353-42-4 164670-44-4 175277-10-8
180403-26-3 206761-87-7 282715-65-5 618913-44-3 848354-08-5
848354-09-6, 1H-Imidazole-2-carbonyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT 848354-05-2P 848354-06-3P 848354-07-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

IT 543-27-1, Iso-butyl chloroformate
RL: RGT (Reagent); RACT (Reactant or reagent)
(preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivs. as androgen receptor modulators and their therapeutic uses)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 5 OF 160 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:58320 CAPLUS
DOCUMENT NUMBER: 142:156210
TITLE: Preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivatives as androgen receptor modulators
INVENTOR(S): Dankulich, William P.; Kaufman, Mildred L.; Meissner, Robert S.; Mitchell, Helen J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

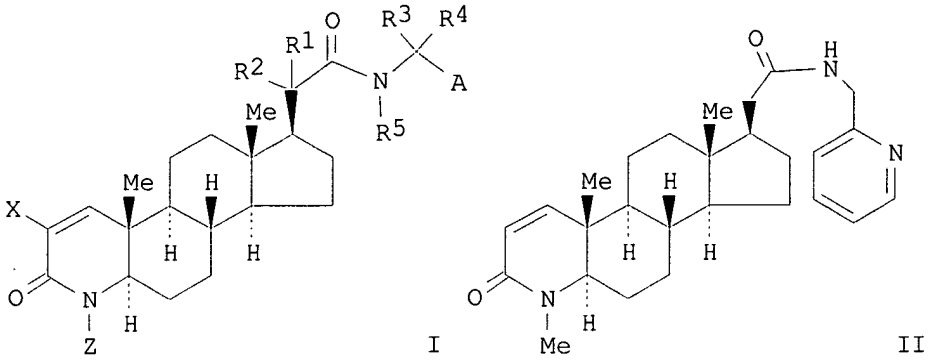
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005005606 | A2 | 20050120 | WO 2004-US20539 | 20040625 |
| WO 2005005606 | A3 | 20050602 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-483675P P 20030630

OTHER SOURCE(S): MARPAT 142:156210

GI



I II

AB 3-Oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs., such as I [X = H, halo; Z = H, CF3, carbonylalkyl, alkyl, alkoxy, halo, CH2OH; A = aromatic ring having 0-4 heteroatoms; polycyclic ring system having one or more aromatic rings and 0-4 heteroatoms; R1, R2, R3, R4, R5 = H, halo, alkyl, amino, alkylamino, aminoalkyl, alkoxyalkyl, alkoxyalkyl, alkoxycarbonylalkyl, cyano, perfluoroalkyl, alkylcarbonyl, alkylcarbonylamino, etc.; R1R2, R3R4 = oxo, spirocycloalkyl], or a pharmaceutically acceptable salt or an enantiomer thereof, were prepared for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivative II, was prepared via a multiple step reaction sequence starting from 4-methyl-3-oxo-4-aza-5α-androst-1-ene-17-carboxylic acid and 2-aminomethylpyridine. I are therefore useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, **aging** skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, **HIV**-wasting, prostate cancer, benign prostatic hyperplasia (BPH), cancer **cachexia**, Alzheimer's disease, muscular dystrophies, cognitive decline, sexual dysfunction, sleep apnea, depression, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(2, bone strengthening agents as adjuvant therapeutics; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(3, bone strengthening agents as adjuvant therapeutics; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(5, bone strengthening agents as adjuvant therapeutics; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(6, bone strengthening agents as adjuvant therapeutics; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as

androgen receptor modulators and their therapeutic uses)

IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(7, bone strengthening agents as adjuvant therapeutics; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Animal cell line
(Hep G2; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Insulin-like growth factor-binding proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IGFBP-3, bone strengthening agents as adjuvant therapeutics; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Peroxisome
(activator of peroxisome proliferator-activated receptor γ as adjuvant therapeutics; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Skin, disease
(**aging**; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Prostacyclin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonist as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Anemia (disease)
(aplastic; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Steroids, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(azasteroids; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Prostate gland, disease
(benign hyperplasia; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Hyperplasia
(benign prostatic; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Antiestrogens
Bone morphogenetic proteins
Estrogens
Progestogens
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bone strengthening agents as adjuvant therapeutics; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Receptors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(calcium, antagonist, bone strengthening agents as adjuvant therapeutics; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT **Cachexia**
(cancerous; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic

uses)
IT Mental and behavioral disorders
(depression; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)
IT Prostaglandins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(derivative, bone strengthening agents as adjuvant therapeutics; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)
IT Ovary, disease
(failure, premature; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)
IT Salts, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fluoride, bone strengthening agents as adjuvant therapeutics; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)
IT Bone, disease
(fracture; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)
IT Lipids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hyperlipidemia; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)
IT Disease, animal
(hypocholesterolemia; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)
IT Testis, disease
(hypogonadism; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)
IT Estrogen receptors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(modulator as adjuvant therapeutics; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)
IT Drug delivery systems
(nasal sprays; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)
IT Bone, disease
(osteopenia; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)
IT Surgery
(plastic, bone; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)
IT Alzheimer's disease
Arthritis
Atherosclerosis
Autoimmune disease
Cognitive disorders
Hematopoietic disorders
Human
Muscular dystrophy
Obesity
Osteoarthritis
Osteoporosis
Periodontium, disease

Prostate gland, neoplasm
Rheumatoid arthritis
Sexual disorders
Sleep apnea
(preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Androgen receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Muscle
(sarcopenia; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Prostanoid receptors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type EP1, agonist as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type EP2, agonist as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type EP4, agonist as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type FP, agonist as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Collagens, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type I, C-telopeptide, as bone turnover marker; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Collagens, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type I, N-telopeptide cross links of type I collagen (NTX), DXA, and DPD as bone turnover marker; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Collagens, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type I, N-telopeptide, as bone turnover marker; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Osteoclast
(vacuolar ATPase inhibitor as adjuvant therapeutics; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT **AIDS** (disease)
(wasting; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Integrins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(αvβ3, receptor antagonist as adjuvant therapeutics; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Transforming growth factors

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β-, bone strengthening agents as adjuvant therapeutics; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 106096-92-8, AFGF 106096-93-9, BFGF
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(agonist as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 50-28-2, 17β-Estradiol, biological studies 53-16-7, Estrone, biological studies 64-96-0, U-11,555A 67-96-9, Dihydrotachysterol 67-98-1, Mer-25 68-22-4, Norethindrone 71-58-9, Medroxyprogesterone acetate 911-45-5, **Clomiphene** 1845-11-0, Nafoxidene 2809-21-4, Etidronate 4717-38-8, 17β-Ethynyl estradiol 5863-35-4, CI-628 7681-49-4, Sodium fluoride, biological studies 9002-64-6, Parathyroid hormone 9007-12-9, Calcitonin 10540-29-1, Tamoxifen 10596-23-3, Clodronate 15690-55-8, Zuclomiphene 15690-57-0, **Enclomiphene** 19356-17-3, 25-Hydroxy-vitamin D3 20859-36-3, Monosodium fluorophosphate 32222-06-3, 1α-25-Dihydroxy-vitamin D3 35212-22-7, Ipriflavone 40391-99-9, Pamidronate 41294-56-8, 1α-Hydroxy-vitamin D3 47931-85-1, Salmon calcitonin 54573-75-0, 1α-Hydroxy-vitamin D2 56287-31-1, CI-680 57333-95-6 57333-96-7 61912-98-9, Insulin, like growth factor 66376-36-1, Alendronate 67763-96-6, IGF I 67763-97-7, IGF II 68893-82-3, Human parathyroid hormone 75330-75-5, Lovastatin 75755-07-6, Piridronate 78994-23-7, Levormeloxifene 79778-41-9, Neridronate 79902-63-9, Simvastatin 81093-37-0, Pravastatin 82413-20-5, Droloxifene 83805-11-2 84449-90-1, Raloxifene 89778-26-7, Toremifene 89987-06-4, Tiludronate 93957-54-1, Fluvastatin 103909-75-7, 22-Oxacalcitriol 104121-92-8, ED71 105462-24-6, Risedronate 112965-21-6, Calcipotriol 114084-78-5, Ibandronate 116057-75-1, Idoxifene 118072-93-8, Zoledronate 118694-43-2, Ro 23-7553 121009-77-6 121268-17-5, Alendronate monosodium trihydrate 121368-58-9, Olpadronate 130447-37-9, 19-Nor-1α-25-dihydroxy-vitamin D3 131875-08-6, KH1060 134404-52-7, EB1089 134523-00-5, Atorvastatin 134523-84-5, 20-epi-1α-25-Dihydroxy-vitamin D3 138330-18-4, Incadronate 141750-63-2, Nisvastatin 145599-86-6, Cerivastatin 147511-69-1, Pitavastatin 180064-38-4, Minodronate 180916-16-9, Lasofoxifene 182133-25-1, Arzoxifene 182167-02-8, EM-652 182167-03-9, EM-800 193830-08-9, GDF5 198481-33-3, TSE 424 205944-50-9, Osteoprotegerin 260055-05-8, Alendronate monosodium monohydrate 287714-41-4, Rosuvastatin 304853-26-7, Growth hormone secretagogue 629704-96-7, Growth hormone, human 797050-81-8, U-100A
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bone strengthening agents as adjuvant therapeutics; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 1406-16-2, Vitamin D 12001-79-5, Vitamin K
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(derivative, bone strengthening agents as adjuvant therapeutics; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 471-34-1, Calcium carbonate, biological studies 7440-70-2, Calcium, biological studies 7693-13-2, Calcium citrate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dietary calcium supplement, bone strengthening agents as adjuvant therapeutics; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 9028-35-7, HMG-CoA reductase 94716-09-3, Cathepsin K
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor as adjuvant therapeutics; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor

modulators and their therapeutic uses)

IT 127464-60-2, Vascular endothelial growth factor
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor of VEGF binding to osteoclast receptors as adjuvant therapeutics; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 165245-96-5, P 38 Kinase
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor, bone strengthening agents as adjuvant therapeutics; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 9000-83-3, ATPase
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(osteoclast vacuolar ATPase inhibitor as adjuvant therapeutics; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 828241-44-7P 828241-45-8P 828241-46-9P 828241-47-0P 828241-48-1P
828241-49-2P 828241-50-5P 828241-51-6P 828241-52-7P 828241-53-8P
828241-54-9P 828241-55-0P 828241-56-1P 828241-57-2P 828241-58-3P
828241-59-4P 828241-60-7P 828241-61-8P 828241-62-9P 828241-63-0P
828241-64-1P 828241-65-2P 828241-66-3P 828241-67-4P 828241-68-5P
828241-69-6P 828241-70-9P 828241-71-0P 828241-72-1P 828241-73-2P
828241-74-3P 828241-75-4P 828241-76-5P 828241-77-6P 828241-78-7P
828241-79-8P 828241-80-1P 828241-81-2P 828241-82-3P 828241-83-4P
828241-84-5P 828241-85-6P 828241-86-7P 828241-87-8P 828241-88-9P
828241-89-0P 828241-90-3P 828241-91-4P 828241-92-5P 828241-93-6P
828241-94-7P 828241-95-8P 828241-96-9P 828241-97-0P 828241-98-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 89-97-4 95-00-1 100-46-9, Benzenemethanamine, reactions 102-49-8
104-84-7 140-75-0 2393-23-9 2740-83-2 3048-01-9 3300-51-4
3468-17-5, 1H-Indole-6-methanamine 3731-51-9, 2-Pyridinemethanamine
3731-52-0, 3-Pyridinemethanamine 3731-53-1, 4-Pyridinemethanamine
4152-90-3 5071-96-5 5760-20-3, 2-Quinolinemethanamine 5805-57-2,
1H-Benzimidazole-2-methanamine 6627-60-7 6850-57-3 16188-30-0,
4-Thiazolemethanamine 19293-58-4 21035-59-6 29096-76-2 39989-43-0
42088-91-5 45588-79-2, 4-Pyrimidinemethanamine 50921-45-4
53332-80-2, 1H-Imidazole-2-methanamine 72235-56-4 73042-50-9
75985-45-4, 2-Pyrimidinemethanamine 81881-74-5, 1H-Indole-5-methanamine
89219-03-4 96692-02-3 98997-01-4 132664-85-8 145490-75-1,
N-Fluorobenzenesulfonamide 153936-26-6 175205-64-8 175530-52-6
214471-76-8 273399-95-4 312904-51-1 332883-10-0 387350-39-2
446829-97-6 500305-98-6 608515-12-4 744187-03-9,
1H-Pyrazolo[3,4-c]pyridine-5-methanamine 759447-33-1 828241-99-2
828242-01-9 828242-02-0 828242-03-1, 1H-Imidazo[4,5-b]pyridine-2-methanamine 828245-44-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 827039-84-9P 827039-85-0P 827039-86-1P 827039-87-2P 827589-72-0P
827589-73-1P 827589-74-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

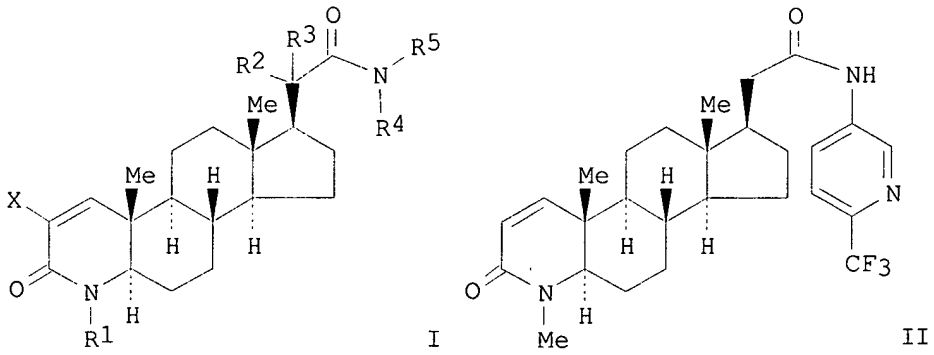
L23 ANSWER 6 OF 160 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:55196 CAPLUS
DOCUMENT NUMBER: 142:156209
TITLE: Preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivatives as androgen receptor modulators

INVENTOR(S): Dankulich, William P.; Kaufman, Mildred L.; Meissner, Robert S.; Mitchell, Helen J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 158 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005005380 | A2 | 20050120 | WO 2004-US20548 | 20040625 |
| WO 2005005380 | A3 | 20050602 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-483784P P 20030630
OTHER SOURCE(S): MARPAT 142:156209
GI




AB 3-Oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs., such as I [X = H, halo; R1 = H, CF3, alkyl, alkoxy, halo, amino, alkylamino, CH2OH; R2, R3 = H, halo, alkyl, amino, aminoalkyl, alkoxyalkyl, alkoxyalkyl, alkoxycarbonylalkyl, cyano, perfluoroalkyl, alkylcarbonyl, alkylcarbonylamino; R2R3 = oxo, spirocycloalkyl; R4, R5 = H, halo, alkyl, alkenyl, alkynyl, carbonylalkyl, carbonylalkenyl, carbonylalkynyl, cycloalkyl, heterocyclyl, cycloheteroalkyl, carboxyaryl, etc.], or a pharmaceutically acceptable salt or an enantiomer thereof, were prepared for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivative II, was prepared via a multiple step reaction sequence starting from 4-methyl-3-oxo-4-aza-5α-androst-1-ene-17-carboxylic acid and 3-amino-6-trifluoromethylpyridine. The prepared compds. are useful as agonists of the androgen receptor in bone and/or muscle tissue while antagonizing the AR in the prostate of a male patient or in the uterus of a female patient. I are therefore useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, **aging** skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic

disorders, inflammatory arthritis and joint repair, **HIV**-wasting, prostate cancer, cancer **cachexia**, Alzheimer's disease, muscular dystrophies, cognitive impairment, decreased libido, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(2, as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(3, as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(5, as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(6, as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(7, as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Animal cell line
(Hep G2; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Skin, disease
(**aging**; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Osteoclast
(an antagonist of VEGF binding to osteoclast receptors as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Anemia (disease)
(aplastic; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Antiestrogens
(as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Prostacyclin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Steroids, preparation
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(azasteroids; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Prostate gland, disease

(benign hyperplasia; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Hyperplasia
(benign prostatic; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Receptors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(calcium, antagonist as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT **Cachexia**
(cancerous; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Mental and behavioral disorders
(depression; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Estrogens
Prostaglandins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(derivative as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Salts, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fluoride, as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Bone, disease
(fracture; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hyperlipidemia; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Testis, disease
(hypogonadism, male; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor of BMP antagonism as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Drug delivery systems
(injections, s.c.; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Estrogen receptors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(modulator as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Drug delivery systems
(nasal sprays; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Bone, disease
(osteopenia; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-

acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Surgery
(plastic, bone; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Alzheimer's disease
Arthritis
Atherosclerosis
Autoimmune disease
Bone formation
Cognitive disorders
Hematopoietic disorders
Human
Hypercholesterolemia
Muscular dystrophy
Obesity
Osteoporosis
Periodontium, disease
Prostate gland, neoplasm
Sexual disorders
Sleep apnea
(preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Androgen receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Androgens
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Muscle
(sarcopenia; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Prostanoid receptors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type EP1, as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type EP2, as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type EP4, as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type FP, as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT **AIDS** (disease)
(wasting; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Integrins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(αvβ3, antagonist as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Transforming growth factors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β-, as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT Peroxisome proliferator-activated receptors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(γ, an activator, as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 1406-16-2, Vitamin D
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(and its derivates as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 7681-49-4, Sodium fluoride, biological studies 20859-36-3, Monosodium fluorophosphate 121268-17-5, Alendronate monosodium trihydrate 260055-05-8, Alendronate monosodium monohydrate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 50-28-2, Estra-1,3,5(10)-triene-3,17-diol (17β)-, biological studies 53-16-7, Estrone, biological studies 67-96-9, Dihydrotachysterol 67-98-1, Mer-25 68-22-4, Norethindrone 71-58-9, Medroxyprogesterone acetate 911-45-5, **Clomiphene** 1845-11-0, Nafoxidene 2809-21-4 4717-38-8, 17β-Ethynyl estradiol 5863-35-4, CI-628 9002-64-6, Parathyroid hormone 9007-12-9, Calcitonin 10540-29-1, Tamoxifen 10596-23-3 15690-55-8, Zuclomiphene 15690-57-0, **Enclomiphene** 19356-17-3, 25-Hydroxy-vitamin D3 32222-06-3, 1α,25-Dihydroxy-vitamin D3 35212-22-7, Ipriflavone 40391-99-9 41294-56-8 50948-44-2, U-11, biological studies 52232-67-4, Human parathyroid hormone (1-34) 54573-75-0, 1α-OH-vitamin D2 56287-31-1, CI-680 57333-95-6 57333-96-7 61912-98-9, Insulin, like growth factor 62031-54-3, Fibroblast growth factor 66376-36-1, Alendronate 67763-96-6, IGF I 67763-97-7, IGF II 68893-82-3, Human parathyroid hormone (1-84) 75330-75-5, Lovastatin 75755-07-6 78994-23-7, Levormeloxifene 79778-41-9, Neridronate 79902-63-9, Simvastatin 81093-37-0, Pravastatin 82413-20-5, Droloxifene 83805-11-2 84449-90-1, Raloxifene 89778-26-7, Toremifene 89987-06-4, Tiludronate 93957-54-1, Fluvastatin 103909-75-7, 22-Oxacalcitriol 104121-92-8, ED71 105462-24-6 112965-21-6, Calcipotriol 114084-78-5, Ibandronate 116057-75-1, Idoxifene 118072-93-8, Zoledronate 118694-43-2, Ro 23-7553 121009-77-6, Dihydroxy open acid simvastatin 121368-58-9, Olpadronate 130447-37-9 131875-08-6, KH1060 134404-52-7, EB1089 134523-00-5, Atorvastatin 134523-84-5 138330-18-4, Incadronate 141750-63-2, Nisvastatin 145599-86-6, Cerivastatin 147511-69-1, Pitavastatin 180064-38-4 180916-16-9, Lasofoxifene 182133-25-1, Arzoxifene 182167-02-8, EM-652 182167-03-9, EM-800 193830-08-9, GDF5 198481-33-3, TSE-424 205944-50-9, Osteoprotegrin 287714-41-4, Rosuvastatin 797050-81-8, U-100A
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 12001-79-5, Vitamin K
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(derivative as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 471-34-1, Calcium carbonate, biological studies 7693-13-2, Calcium citrate
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(dietary calcium supplement as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 9002-72-6, Growth hormone
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human growth hormone as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 9028-35-7, HMG-CoA reductase 94716-09-3, Cathepsin K 165245-96-5, p38 Kinase
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 127464-60-2, Vascular endothelial growth factor
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of VEGF binding to osteoclast receptors as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 57-83-0, Progestin, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(or its derivative as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 9000-83-3, ATPase
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(osteoclast vacuolar, inhibitor as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 827581-16-8P 827581-18-0P 827581-20-4P 827581-22-6P 827581-24-8P
827581-26-0P 827581-28-2P 827581-30-6P 827581-32-8P 827581-34-0P
827581-36-2P 827581-38-4P 827581-40-8P 827581-42-0P 827581-44-2P
827581-46-4P 827581-48-6P 827581-50-0P 827581-52-2P 827581-54-4P
827581-56-6P 827581-58-8P 827581-60-2P 827581-62-4P 827581-64-6P
827581-66-8P 827581-68-0P 827581-70-4P 827581-72-6P 827581-74-8P
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827585-18-2P 827585-20-6P 827585-21-7P 827585-24-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 827585-27-3P 827585-29-5P 827585-30-8P 827585-33-1P 827585-35-3P
827585-38-6P 827585-41-1P 827585-44-4P 827585-47-7P 827585-50-2P
827585-51-3P 827585-53-5P 827585-55-7P 827585-57-9P 827589-83-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 47931-85-1, Salmon calcitonin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 54-96-6, 3,4-Pyridinediamine 61-80-3 62-53-3, Benzenamine, reactions
95-51-2 95-54-5, 1,2-Benzenediamine, reactions 95-83-0 96-50-4,
2-Thiazolamine 98-16-8 98-59-9, p-Toluenesulfonyl chloride 102-51-2
104-94-9 106-47-8, reactions 106-49-0, reactions 108-42-9 108-52-1
109-12-6, 2-Pyrimidinamine 141-86-6, 2,6-Pyridinediamine 143-33-9,
Sodium cyanide 329-89-5 360-97-4 367-31-7 368-71-8 371-40-4
372-19-0 372-39-4 452-58-4, 2,3-Pyridinediamine 455-14-1 461-82-5
461-98-3 462-08-8, 3-Pyridinamine 496-72-0 504-24-5, 4-Pyridinamine
504-29-0, 2-Pyridinamine 536-90-3 591-54-8, 4-Pyrimidinamine
591-55-9, 5-Pyrimidinamine 695-34-1 769-27-7 824-94-2,
p-Methoxybenzyl chloride 873-74-5 934-32-7, 1H-Benzimidazol-2-amine
1072-67-9 1072-97-5 1072-98-6 1603-40-3 1603-41-4 1603-91-4
1633-42-7 1820-80-0, 1H-Pyrazol-3-amine 1824-81-3 1827-27-6
1990-90-5 2237-30-1 2289-75-0 2587-02-2 2687-25-4 2835-68-9
2941-62-0 3167-49-5 3430-14-6 3544-24-9 3676-85-5 4214-73-7
4318-76-7, 2,5-Pyridinediamine 4318-79-0, 2,3,6-Pyridinetriamine
4418-61-5, 1H-Tetrazol-5-amine 5049-61-6, Pyrazinamine 5350-93-6
5398-36-7 5407-87-4 5509-65-9 6298-37-9, 6-Quinoxalinamine
6628-04-2 6628-77-9 7305-71-7 7720-39-0, 1H-Imidazol-2-amine
7749-47-5 10444-89-0 13538-41-5 13566-35-3 13754-19-3,
4,5-Pyrimidinediamine 14150-95-9 14432-12-3 14678-02-5 16250-08-1
17467-35-5 18437-58-6 19335-11-6, 1H-Indazol-5-amine 19798-81-3
19947-75-2 21717-29-3 21717-96-4 22715-27-1, 2,5-Pyrimidinediamine
22715-28-2 22889-78-7 24340-76-9 24638-29-7 28020-37-3
29958-14-3 31230-17-8 31860-60-3, [2,3'-Bipyridin]-6'-amine
31970-30-6, [3,3'-Bipyridin]-6-amine 33259-72-2 33630-94-3
36052-24-1 36692-49-6 39658-41-8 39889-94-6 40283-41-8
41663-73-4 41995-31-7 42753-71-9 50850-16-3 52334-90-4
53929-59-2 55338-73-3 55809-36-4 57187-73-2 57235-50-4
65367-69-3 74784-70-6 75308-73-5 79739-33-6, [3,4'-Bipyridin]-6-amine 81633-29-6 82039-90-5 86283-81-0 94924-86-4 96692-02-3
103335-41-7 104685-76-9 106877-33-2 107582-20-7 107867-51-6
118452-02-1 126553-00-2 128293-62-9 133745-75-2 145255-19-2
159485-75-3 218631-50-6 263710-28-7 449796-46-7 827585-96-6
827585-99-9 827586-03-8 827586-90-3 827587-17-7 827587-90-6
827587-92-8 827587-96-2 827587-99-5 827588-01-2 827588-04-5
827588-06-7 827588-09-0 827588-12-5 827588-15-8 827588-17-0
827588-24-9 827588-33-0 827588-36-3 827588-38-5 827588-49-8

827588-52-3 827588-55-6 827588-62-5 827588-67-0 827588-72-7
827588-81-8 827588-84-1 827588-87-4 827588-90-9 827588-93-2
827589-03-7 827589-07-1 827589-12-8 827589-15-1 827589-18-4
827589-21-9 827589-24-2 827589-29-7 827589-38-8 827589-79-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 606101-77-3P 606101-78-4P 606101-79-5P 827039-84-9P 827039-85-0P
827039-86-1P 827039-87-2P 827589-62-8P 827589-63-9P 827589-64-0P
827589-65-1P 827589-66-2P 827589-67-3P 827589-68-4P 827589-69-5P
827589-70-8P 827589-71-9P 827589-72-0P 827589-73-1P 827589-74-2P
827589-75-3P 827589-76-4P 827589-77-5P 827589-78-6P 827589-80-0P
827589-81-1P 827589-82-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 603-35-0D, Triphenyl phosphine, polystyrene bound
RL: RGT (Reagent); RACT (Reactant or reagent)
(preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

IT 7440-70-2, Calcium, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(supplement as adjuvant bone strengthening agents; preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs. as androgen receptor modulators and their therapeutic uses)

L23 ANSWER 7 OF 160 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:55024 CAPLUS
DOCUMENT NUMBER: 142:134783
TITLE: 17-Acetamido-4-azasteroid derivatives as androgen receptor modulators for the treatment of related diseases
INVENTOR(S): Dankulich, William P.; Meissner, Robert S.; Mitchell, Helen J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005004807 | A2 | 20050120 | WO 2004-US20753 | 20040625 |
| WO 2005004807 | A3 | 20050407 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-483664P P 20030630
OTHER SOURCE(S): MARPAT 142:134783
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB 17-Acetamido-4-azasteroid derivs., I (X = H or halogen; R1 = H, CF3, CO,

C1-3 alkyl, C1-4 alkoxy, halogen , hydroxymethyl, wherein said alkyl, and alkoxy are optionally substituted with 1-7 F atoms; Y = a substituted or unsubstituted hetercycle containing at least one nitrogen; R2, R3 = H, halogen, C1-8 alkyl, aminoalkyl, hydroxycarbonyl, CN, OH, etc.) were prepared as androgen receptor modulators for the treatment of related diseases. Thus, II was treated with Et3N, and iso-Bu chloroformate, followed by LiBH4 to give the alchol. This alc. was converted to the tosylate, which was converted to the nitrile. Oxidation of the nitrile resulted in formation of the corresponding acid which was treated with 2-oxopiperizine, EDC, and HOAt to give III.

IT Insulin-like growth factor-binding proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IGFBP-3; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonist; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Anemia (disease)
(aplastic, treatment of; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Prostate gland, disease
(benign hyperplasia, treatment of; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Hyperplasia
(benign prostatic, treatment of; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(calcium, antagonist; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Mental and behavioral disorders
(depression, treatment of; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Prostaglandins
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(derivs.; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Bone, disease
(fracture, treatment of; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hyperlipidemia, treatment of; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Reproductive system, disease
(hypogonadism, treatment of; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Androgen receptors
Estrogen receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulators; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Bone, disease
(osteopenia, treatment of; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Drug delivery systems
Drug discovery
Human
(preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Bone morphogenetic proteins
Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor

modulators and treatment of related diseases)

IT Antiestrogens
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Muscle
(sarcopenia, treatment of; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Menopause
(treatment of symptoms; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Alzheimer's disease
Arthritis
Atherosclerosis
Autoimmune disease
Bone, disease
**Cachexia**
Hematopoietic disorders
Hypercholesterolemia
Muscular dystrophy
Neoplasm
Obesity
Osteoporosis
Periodontium, disease
Prostate gland, neoplasm
Sexual disorders
Sleep apnea
(treatment of; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Transforming growth factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β-; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(γ, activator of; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT 127464-60-2, Vascular endothelial growth factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonist; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT 12001-79-5P, Vitamin k
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(derivs.; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT 73984-05-1, BMP
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor of antagonism; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT 9028-35-7, HMG-CoA reductase 94716-09-3, Cathepsin K
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor of; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT 9002-64-6, Parathyroid hormone 9002-72-6, Human growth hormone 9007-12-9, Calcitonin 61912-98-9, Insulin-like growth factor 67763-96-6, IGF I 67763-97-7, IGF II 106096-92-8, AFGF 106096-93-9, BFGF 192509-82-3, BMP 2 192509-86-7, BMP 3 193830-08-9, GDF5
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT 35212-22-7P, Ipriflavone 205944-50-9P, Osteoprotegerin 827039-75-8P 827039-76-9P 827039-77-0P 827039-78-1P 827039-79-2P 827039-80-5P 827039-81-6P 827039-82-7P 827039-83-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT 50-28-2, Estra-1,3,5(10)-triene-3,17-diol (17β)-, biological studies 53-16-7, Estrone, biological studies 64-96-0, U 11555A 67-96-9, Dihydrotachysterol 67-98-1, Mer 25 68-22-4, Norethindrone 71-58-9, Medroxyprogesterone acetate 471-34-1, Calcium carbonate, biological studies 911-45-5, **Clomiphene** 1406-16-2, Vitamin D 1845-11-0, Nafoxidene 2809-21-4 4717-38-8, 17β-Ethynyl estradiol 5863-35-4, CN 55945-27 7693-13-2, Calciumcitrate 10540-29-1, Tamoxifen 10596-23-3 15690-55-8, Zuclomiphene 15690-57-0, **Enclomiphene** 19356-17-3, 25-Hydroxy-vitamin D3 40391-99-9 41294-56-8 54573-75-0 56287-31-1, CI 680 66376-36-1, Alendronate 75330-75-5, Lovastatin 75755-07-6 78994-23-7, Levormeloxifene 79778-41-9, Neridronate 79902-63-9, Simvastatin 81093-37-0, Pravastatin 82413-20-5, Droloxifene 84449-90-1, Raloxifene 89778-26-7, Toremifene 89987-06-4, Tiludronate 93957-54-1, Fluvastatin 103909-75-7, 22-Oxacalcitriol 104121-92-8, ED 71 105462-24-6 114084-78-5, Ibandronate 116057-75-1, Idoxifene 118072-93-8, Zoledronate 121268-17-5, Alendronate monosodium trihydrate 121368-58-9, Olpadronate 130447-37-9, 19-Nor-1α,25 dihydroxyvitamin D3 131875-08-6, KH 1060 134404-52-7, EB 1089 134523-00-5, Atorvastatin 138330-18-4, Incadronate 141750-63-2, Nisvastatin 145599-86-6, Cerivastatin 147511-69-1, Pitavastatin 163659-89-0, 1α,25-Dihydroxy-16-ene-23-yne-vitamin D3 180064-38-4 180916-16-9, Lasofoxifene 182167-02-8, EM 652 182167-03-9, EM 800 198481-33-3, TSE 424 260055-05-8, Alendronate monosodium monohydrate 287714-41-4, Rosuvastatin 797050-81-8, U 100A (pharmaceutical)
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT 5625-67-2, Piperazinone 96692-02-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT 827039-84-9P 827039-85-0P 827039-86-1P 827039-87-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

L23 ANSWER 8 OF 160 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1311659 CAPLUS
DOCUMENT NUMBER: 144:51330
TITLE: N-benzyl-2-phenylbutanamides as tissue-selective androgen receptor modulators, their preparation, pharmaceutical compositions, and use in therapy
INVENTOR(S): Hanney, Barbara; Kim, Yuntae; Krout, Michael R.; Meissner, Robert S.; Mitchell, Helen J.; Musselman, Jeffrey; Perkins, James J.; Wang, Jiabing
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 50 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

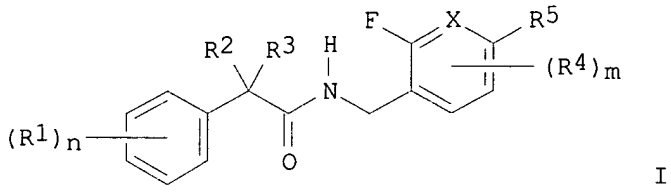
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2005277681 | A1 | 20051215 | US 2005-145490 | 20050603 |
| WO 2005120477 | A2 | 20051222 | WO 2005-US19554 | 20050603 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

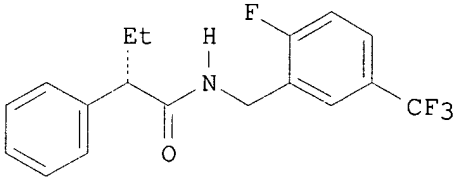
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-577698P P 20040607

GI



I



II

AB The invention relates to compds. of structural formula I, which are modulators of the androgen receptor (AR) in a tissue-selective manner. In compds. I, X is CH or N; n is 0, 1, 2, or 3; m is 0, 1, or 2; R1, R4, and R5 are independently selected from H, halo, cyano, (un)substituted C1-10 alkyl, (un)substituted C2-10 alkenyl, (un)substituted aryl-C0-10 alkyl, (un)substituted perfluoro-C1-6 alkyl, etc.; R2 and R3 are independently selected from H, halo, cyano, amino, hydroxy-C0-10 alkyl, (un)substituted C1-10 alkyl, (un)substituted C2-10 alkenyl, (un)substituted aryl-C0-10 alkyl, (un)substituted perfluoro-C1-6 alkyl, etc. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of a compound I and a pharmaceutically acceptable carrier, as well as to the use of the compns. for the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration. Coupling of (S)-2-phenylbutanoic acid with 2-fluoro-5-(trifluoromethyl)benzylamine gave butanamide II. Compds. of the invention, e.g., II, express affinity for endogenously expressed androgen receptor with IC50 values of 1 μM or less.

IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(2; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(3; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(5; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(6; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT Bone morphogenetic proteins

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(7; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT Insulin-like growth factor-binding proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IGFBP-3; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT Obesity
(abdominal; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT Bone mineral density
(agents increasing; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT Skin, disease
(**aging**; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT Antiarteriosclerotics
(antiatherosclerotics; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT Anemia (disease)
(aplastic; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT Drugs
(appetite stimulants; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT Prostate gland, disease
(benign hyperplasia; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT Hyperplasia
(benign prostatic; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT Surgery
(bone damage following bone reconstructive; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(calcium; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT **Cachexia**
(cancerous; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT Drug delivery systems
(carriers; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT Mental and behavioral disorders
(depression; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT Bone, disease
(fracture; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hyperlipidemia; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT Reproductive system, disease
(hypogonadism, male; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT Drug delivery systems
(injections, s.c.; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT Disease, animal
(metabolic syndrome X; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT Drug delivery systems
(nasal sprays; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT Diabetes mellitus

(non-insulin-dependent; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)
IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(osteoclast; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)
IT Menopause
(postmenopause; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)
IT Ovary, disease
(premature ovarian failure; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)
IT **AIDS** (disease)
Alzheimer's disease
Anti-Alzheimer's agents
Antiarthritics
Anticholesteremic agents
Antidepressants
Antidiabetic agents
Antiestrogens
Antiobesity agents
Antiosteoporotic agents
Antitumor agents
Arthritis
Atherosclerosis
Autoimmune disease
Bone
Bone resorption inhibitors
Cognition enhancers
Cognitive disorders
Combination chemotherapy
Equus caballus
Hematopoietic disorders
Human
Human immunodeficiency virus
Human immunodeficiency virus 1
Hypercholesterolemia
Hypolipemic agents
Muscle
Muscular dystrophy
Obesity
Osteoclast
Osteoporosis
Periodontium, disease
Prostate gland
Prostate gland, neoplasm
Rheumatoid arthritis
Sexual disorders
Sleep apnea
Uterus
(preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)
IT Androgen receptors
Prostacyclin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)
IT Androgens
Estrogens
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)
IT Bone morphogenetic proteins
Prostaglandins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)
IT Androgens
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(replacement therapy; preparation of N-benzyl-phenylbutanamides as androgen

receptor modulators)
IT Muscle
(sarcopenia; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)
IT Estrogen receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(selective modulator of; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)
IT Appetite
(stimulants; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)
IT Diet
(supplements, calcium; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)
IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type EP1; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)
IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type EP2; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)
IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type EP4; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)
IT Collagens, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type I, C-telopeptide, degradation products of; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)
IT Collagens, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type I, N-telopeptide, urinary, crosslinks of; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)
IT Disease, animal
(wasting, **HIV**-associated; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)
IT Muscle, disease
(weakened muscle tone; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)
IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(αvβ3; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)
IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(αvβ3; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)
IT Transforming growth factors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β-; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)
IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(γ, calcium; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)
IT 13598-36-2D, Phosphonic acid, alkylidenebis- derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Bisphosphonate; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)
IT 871325-24-5P, (S)-N-(5-Bromo-2-fluorobenzyl)-2-phenylbutanamide
871325-35-8P, N-(5-Bromo-2-fluorobenzyl)-2-phenylbutanamide
871325-59-6P, (R)-3,3,3-Trifluoro-N-(3-bromo-2-fluoro-5-trifluoromethylbenzyl)-2-hydroxy-2-phenylpropanamide
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(drug candidate; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT 871325-11-0P, (S)-N-[2-Fluoro-5-(trifluoromethyl)benzyl]-2-phenylbutanamide 871325-12-1P, N-(2-Fluoro-5-methylbenzyl)-2-phenylbutanamide 871325-19-8P, (2S)-N-[[2-Fluoro-5-(trifluoromethyl)pyridin-3-yl]methyl]-2-phenylbutanamide 871325-20-1P, N-[5-(1,1-Difluoroethyl)-2-fluorobenzyl]-2-phenylbutanamide 871325-25-6P, N-[2-Fluoro-5-(trifluoromethyl)benzyl]-2-phenylbutanamide 871325-26-7P, N-(5-Ethyl-2-fluorobenzyl)-2-phenylbutanamide 871325-27-8P, (S)-N-(5-Ethyl-2-fluorobenzyl)-2-phenylbutanamide 871325-28-9P, N-(5-Cyclopropyl-2-fluorobenzyl)-2-phenylbutanamide 871325-29-0P, N-(2-Fluoro-5-vinylbenzyl)-2-phenylbutanamide 871325-30-3P, N-[2-Fluoro-5-(trifluoromethyl)benzyl]-2-(3-fluorophenyl)butanamide 871325-31-4P, N-(5-Ethyl-2-fluorobenzyl)-2-(4-chlorophenyl)butanamide 871325-32-5P, N-[(2-Fluoro-5-methylpyridin-3-yl)methyl]-2-phenylbutanamide 871325-33-6P, (S)-N-[(2-Fluoro-5-methylpyridin-3-yl)methyl]-2-phenylbutanamide 871325-34-7P, (S)-N-[(5-Ethyl-2-fluoropyridin-3-yl)methyl]-2-phenylbutanamide 871325-36-9P, N-(5-Ethyl-2-fluorobenzyl)-2-(3-chlorophenyl)butanamide 871325-37-0P, N-(5-Ethyl-2-fluorobenzyl)-2-(3,4-dichlorophenyl)butanamide 871325-38-1P, (S)-N-[(5-Cyclopropyl-2-fluoropyridin-3-yl)methyl]-2-phenylbutanamide 871325-39-2P, N-[(5-Cyclopropyl-2-fluoropyridin-3-yl)methyl]-2-(3,4-dichlorophenyl)butanamide 871325-40-5P, N-[(5-Ethyl-2-fluoropyridin-3-yl)methyl]-2-(3,4-dichlorophenyl)butanamide 871325-41-6P, N-[(5-Methyl-2-fluoropyridin-3-yl)methyl]-2-(3,4-dichlorophenyl)butanamide 871325-42-7P, N-[2-Fluoro-5-(trifluoromethyl)benzyl]-2-(3-bromophenyl)butanamide 871325-43-8P, N-(5-Bromo-2-fluorobenzyl)-2-(3-bromophenyl)butanamide 871325-44-9P, N-[5-(Cyclopropyl)-2-fluorobenzyl]-2-(3-bromophenyl)butanamide 871325-45-0P, N-(5-Chloro-2-fluorobenzyl)-2-(4-bromophenyl)butanamide 871325-46-1P, N-[2-Fluoro-5-(trifluoromethyl)benzyl]-2-(4-bromophenyl)butanamide 871325-47-2P, N-(5-Bromo-2-fluorobenzyl)-2-(4-bromophenyl)butanamide 871325-48-3P, N-[5-(Cyclopropyl)-2-fluorobenzyl]-2-(4-bromophenyl)butanamide 871325-49-4P, N-[2-Fluoro-5-(trifluoromethyl)benzyl]-2-hydroxy-2-phenylbutanamide 871325-50-7P, N-[2-Fluoro-5-(trifluoromethyl)benzyl]-2-(3-chlorophenyl)-2-hydroxybutanamide 871325-51-8P, N-[(2-Fluoro-5-methylpyridin-3-yl)methyl]-2-hydroxy-2-phenylbutanamide 871325-52-9P, 2-Cyclopropyl-N-[(2-fluoro-5-methylpyridin-3-yl)methyl]-2-hydroxy-2-phenylacetamide 871325-53-0P, N-[(5-Ethyl-2-fluoropyridin-3-yl)methyl]-2-hydroxy-2-phenylbutanamide 871325-54-1P, (R)-3,3,3-Trifluoro-N-[(2-fluoro-5-methylpyridin-3-yl)methyl]-2-hydroxy-2-phenylpropanamide 871325-55-2P, (R)-3,3,3-Trifluoro-N-(2-fluoro-5-trifluoromethylbenzyl)-2-hydroxy-2-phenylpropanamide 871325-56-3P, 2-(4-Chloro-3-fluorophenyl)-3,3,3-trifluoro-N-[2-fluoro-5-(trifluoromethyl)benzyl]-2-hydroxypropanamide 871325-61-0P, (R)-3,3,3-Trifluoro-N-(3-cyano-2-fluoro-5-trifluoromethylbenzyl)-2-hydroxy-2-phenylpropanamide 871325-62-1P, (R)-3,3,3-Trifluoro-N-(4-cyano-5-ethyl-2-fluorobenzyl)-2-hydroxy-2-phenylpropanamide 871325-63-2P, 3,3,4,4,4-Pentafluoro-N-[(2-fluoro-5-methylpyridin-3-yl)methyl]-2-hydroxy-2-phenylbutanamide 871325-64-3P, (2R)-3,3,3-Trifluoro-N-(2-fluoro-5-ethylbenzyl)-2-hydroxy-2-phenylpropanamide 871325-65-4P, (2R)-3,3,3-Trifluoro-N-(2-fluoro-5-bromobenzyl)-2-hydroxy-2-phenylpropanamide 871325-66-5P, (2R)-3,3,3-Trifluoro-N-(2-fluoro-5-chlorobenzyl)-2-hydroxy-2-phenylpropanamide 871325-67-6P, 3,3,4,4,4-Pentafluoro-N-(2-fluoro-5-cyclopropylbenzyl)-2-hydroxy-2-phenylbutanamide 871325-68-7P, 3,3,4,4,4-Pentafluoro-N-(2-fluoro-5-trifluoromethylbenzyl)2-hydroxy-2-phenylbutanamide 871325-69-8P, 3,3,3-Trifluoro-N-(2,3,5-trifluorobenzyl)-2-hydroxy-2-phenylpropanamide 871325-70-1P, 2-(4-Fluorophenyl)-3,3,3-trifluoro-N-[2-fluoro-5-cyclopropylbenzyl]-2-hydroxypropanamide 871325-71-2P, 3-[[2-Fluoro-5-(trifluoromethyl)benzyl]amino]-3-oxo-2-phenylpropyl dimethylcarbamate 871325-73-4P, 3-[[2-Fluoro-5-(trifluoromethyl)benzyl]amino]-3-oxo-2-phenylpropyl pyrrolidine-1-carboxylate 871325-74-5P, 3-[[(2-Fluoro-5-methylpyridin-3-yl)methyl]amino]3-oxo-2-phenylpropyl pyrrolidine-1-carboxylate 871325-75-6P, 3-[[(2-Fluoro-5-methylpyridin-3-yl)methyl]amino]3-oxo-2-phenylpropyl dimethylcarbamate 871325-76-7P, 3-[[2-Fluoro-5-(trifluoromethyl)benzyl]amino]-1-methyl-3-oxo-2-phenylpropyl pyrrolidine-1-carboxylate 871325-77-8P, 3-[[2-Fluoro-5-

(trifluoromethyl)benzyl]amino]-2-hydroxy-3-oxo-2-phenylpropyl pyrrolidine-1-carboxylate 871325-78-9P, N-[3-Fluoro-5-(trifluoromethyl)benzyl]-2-phenylbutanamide 871325-79-0P, (R)-N-[2-Fluoro-5-(trifluoromethyl)benzyl]-2-hydroxy-2-phenylbutanamide 871325-80-3P, (S)-N-[2-Fluoro-5-(trifluoromethyl)benzyl]-2-hydroxy-2-phenylbutanamide 871325-81-4P, (R)-N-[2-Fluoro-5-(trifluoromethyl)benzyl]-2-(3-chlorophenyl)-2-hydroxybutanamide 871325-82-5P, (S)-N-[2-Fluoro-5-(trifluoromethyl)benzyl]-2-(3-chlorophenyl)-2-hydroxybutanamide 871325-83-6P, (R)-N-[(2-Fluoro-5-methylpyridin-3-yl)methyl]-2-hydroxy-2-phenylbutanamide 871325-84-7P, (S)-N-[(2-Fluoro-5-methylpyridin-3-yl)methyl]-2-hydroxy-2-phenylbutanamide 871325-85-8P 871325-86-9P 871325-87-0P, (R)-N-[(5-Ethyl-2-fluoropyridin-3-yl)methyl]-2-hydroxy-2-phenylbutanamide 871325-88-1P, (S)-N-[(5-Ethyl-2-fluoropyridin-3-yl)methyl]-2-hydroxy-2-phenylbutanamide 871325-89-2P, (S)-N-[3-Fluoro-5-(trifluoromethyl)benzyl]-2-phenylbutanamide 871326-46-4P, (2R)-3,3,3-Trifluoro-N-(2-fluoro-5-cyclopropylbenzyl)-2-hydroxy-2-phenylpropanamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT 288309-07-9P, 5-Acetyl-2-fluorobenzonitrile 871325-13-2P, 5-Ethyl-2-fluoropyridine 871325-14-3P, 5-Ethyl-2-fluoropyridine-3-carboxaldehyde 871325-15-4P, (5-Ethyl-2-fluoropyridin-3-yl)methanamine hydrochloride 871325-16-5P 871325-17-6P, (2-Fluoro-5-methylpyridin-3-yl)methanamine 871325-18-7P, (S)-N-[[2-Amino-5-(trifluoromethyl)pyridin-3-yl]methyl]-2-phenylbutanamide 871325-57-4P, 3-Bromo-2-fluoro-5-trifluoromethylbenzylamine 871325-58-5P, 4-Bromo-5-ethyl-2-fluorobenzylamine 871325-60-9P, (R)-3,3,3-Trifluoro-N-(4-bromo-5-ethyl-2-fluorobenzyl)-2-hydroxy-2-phenylpropanamide 871325-72-3P, N-(2-Fluoro-5-trifluoromethylbenzyl)-3-hydroxy-2-phenylpropanamide
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT 9000-83-3, ATPase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(osteoclast vacuolar; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT 9028-35-7, HMGCoA reductase 73984-05-1, BMP 94716-09-3, Cathepsin K 127464-60-2, VEGF 165245-96-5, p38 Protein kinase 372092-80-3, Protein kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT 7440-70-2, Calcium, biological studies
RL: BSU (Biological study, unclassified); FFD (Food or feed use); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT 57-83-0, Progestin, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT 50-28-2, Estra-1,3,5(10)-triene-3,17-diol (17β)-, biological studies 53-16-7, Estrone, biological studies 64-96-0 67-96-9, Dihydrotachysterol 67-98-1, Mer-25 68-22-4, Norethindrone 71-58-9, Medroxyprogesterone acetate 93-05-0, DPD 471-34-1, Calcium carbonate, biological studies 911-45-5, **Clomiphene** 1406-16-2, Vitamin D 1845-11-0, Nafoxidene 2809-21-4 4717-38-8, 17β-Ethynyl estradiol 5863-35-4, CI-628 7681-49-4, Sodium fluoride, biological studies 7693-13-2, Calcium citrate 9002-64-6, Parathyroid hormone 9002-72-6, Somatotropin 9007-12-9, Calcitonin 10540-29-1, Tamoxifen 10596-23-3, Clodronate 12001-79-5, Vitamin K 15690-55-8, Zuclomiphene 15690-57-0, **Enclomiphene** 16984-48-8, Fluoride, biological studies 19356-17-3, 25-Hydroxy-vitamin D3 20859-36-3, Monosodium fluorophosphate 32222-06-3, 1α,25 Dihydroxy vitamin D3 35212-22-7, Ipriflavone 40391-99-9 41294-56-8, 1α-Hydroxy-vitamin D3 47931-85-1, Salmon calcitonin 54573-75-0,

1α-Hydroxy-vitamin D2 56287-31-1, CI-680 57333-95-6 57333-96-7 61912-98-9, Insulin-like growth factor 62031-54-3, Fibroblast growth factor 66376-36-1, Alendronate 67763-96-6, Insulin-like growth factor I 67763-97-7, Insulin-like growth factor II 68893-82-3, Human Parathyroid hormone 75755-07-6 78994-23-7, Levormeloxifene 79778-41-9, Neridronate 79902-63-9, Simvastatin 81093-37-0, Pravastatin 82413-20-5, Droloxifene 83805-11-2, F6-1α,25-Dihydroxy-vitamin D3 84449-90-1, Raloxifene 89778-26-7, Toremifene 89987-06-4, Tiludronate 93957-54-1, Fluvastatin 103909-75-7, 22-Oxacalcitriol 104121-92-8, ED71 105462-24-6 106096-92-8, Acidic fibroblast growth factor 106096-93-9, Basic FGF 112965-21-6, Calcipotriol 114084-78-5, Ibandronate 116057-75-1, Idoxifene 118072-93-8, Zoledronate 121268-17-5, Alendronate monosodium trihydrate 121368-58-9, Olpadronate 130447-37-9, 19-Nor-1α,25-dihydroxy-vitamin D3 131875-08-6, KH1060 134404-52-7, EB1089 134523-00-5, Atorvastatin 134523-84-5 138330-18-4, Incadronate 141750-63-2, Nisvastatin 145599-86-6, Cerivastatin 147511-69-1, Pitavastatin 163659-89-0, 1α,25-Dihydroxy-16-ene-23-yne-vitamin D3 180064-38-4 180916-16-9, Lasofoxifene 182133-25-1, Arzoxifene 182167-02-8, EM-652 182167-03-9, EM-800 193830-08-9, GDF5 198481-33-3, TSE 424 205944-50-9, Osteoprotegerin 260055-05-8, Alendronate monosodium monohydrate 287714-41-4, Rosuvastatin 797050-81-8, U-100A
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

IT 123-75-1, Pyrrolidine, reactions 552-63-6, Tropic acid 587-47-3, Ethyl 3-fluorophenylacetate 611-73-4, 2-Oxo-2-phenylacetic acid 718-08-1 766-11-0, 5-Bromo-2-fluoropyridine 2369-19-9, 2-Fluoro-5-methylpyridine 4286-15-1, (S)-2-Phenylbutanoic acid 13081-18-0, Ethyl trifluoropyruvate 14062-24-9, Ethyl 4-chlorophenylacetate 17257-70-4 36854-57-6, 2-Phenylbutanoyl chloride 74784-70-6, 5-(Trifluoromethyl)pyridin-2-amine 93071-82-0, (2-Fluoro-5-methylphenyl)methanamine 146374-27-8, tert-Butylsulfinamide 190656-34-9, (5-Bromo-2-fluorobenzyl)amine 199296-61-2, [2-Fluoro-5-(trifluoromethyl)phenyl]methanamine 218301-22-5, 2-Fluoro-5-formylbenzonitrile 261723-26-6, (5-Chloro-2-fluorobenzyl)amine 871325-21-2, [[2-Fluoro-5-(trifluoromethyl)pyridin-3-yl]methyl]amine 871325-22-3, [(5-Ethyl-2-fluoropyridin-3-yl)methyl]amine 871325-23-4, [(5-Cyclopropyl-2-fluoropyridin-3-yl)methyl]amine
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of N-benzyl-phenylbutanamides as androgen receptor modulators)

L23 ANSWER 9 OF 160 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:983611 CAPLUS
DOCUMENT NUMBER: 143:292527
TITLE: Bioavailability and improved delivery of alkaline pharmaceutical drugs
INVENTOR(S): Yu, Ruey J.; Van Scott, Eugene J.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 16 pp., Cont.-in-part of U.S. Ser. No. 792,273.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| US 2005196418 | A1 | 20050908 | US 2005-50434 | | 20050204 |
| US 2004214215 | A1 | 20041028 | US 2004-792273 | | 20040304 |
| PRIORITY APPLN. INFO.: | | | US 2004-792273 | A2 | 20040304 |
| | | | US 2003-452557P | P | 20030307 |

OTHER SOURCE(S): MARPAT 143:292527
AB Embodiments of the invention relate to a composition, a process of making the composition, and to the use of the composition The compns. include a mol. complex formed between an alkaline pharmaceutical drug and at least one selected from a hydroxy acid, a polyhydroxy acid, a related acid, a lactone, or

combinations thereof. The compns. provide improved bioavailability and improved delivery of the drug into the cutaneous tissues. For example, diphenhydramine hydrochloride 29 g (0.1 mol) was dissolved in water and 5 N sodium hydroxide generating diphenhydramine free base. Gluconolactone 18 g (0.1 mol) was added to form a mol. complex of 0.1 mol diphenhydramine free base with 0.1 mol gluconic acid/gluconolactone. The solution thus obtained was used for various forms of topical formulations including oil-in-water creams, lotions, gels and solns.

IT Collagens, biological studies
Elastins
Glycosaminoglycans, biological studies
Proteoglycans, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(abnormal syntheses of; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)

IT Acne
Dandruff
Dermatitis
Eczema
Erythema
Gingiva, disease
Hair, disease
Motion sickness
Nail (anatomical), disease
Pruritus
Psoriasis
Seborrhea
Wart
(agents for treatment of; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)

IT Skin, disease
(**aging**, agents for treatment of; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)

IT Carbohydrates, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(aldonic acids; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)

IT Anti-inflammatory agents
Antibacterial agents
Antiemetics
Antihistamines
Antiperspirants
Antiviral agents
Drug bioavailability
Fungicides
Humectants
Keratosis
Sunscreens
Suntanning agents
(bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)

IT Acids, reactions
Lactones
Uronic acids
RL: RCT (Reactant); RACT (Reactant or reagent)
(bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)

IT Corticosteroids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)

IT Hormones, animal, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)

IT Retinoids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)

IT Vitamins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Shale oils
(combination with; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Coal tar
Wood tar
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination with; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Hair preparations
(conditioners; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Skin, disease
(corn, agents for treatment of; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Cosmetics
(depilatories; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Mucous membrane
(disease, agents for treatment of; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Foot
(disease, calus, agents for treatment of; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Skin, disease
(dry, xerosis, agents for treatment of; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Keratosis
(follicularis, agents for treatment of; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Drug delivery systems
(gels; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Infection
Skin, disease
(herpes, agents for treatment of; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Carboxylic acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydroxy; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Keratosis
(hyperkeratosis, agents for treatment of; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Skin, disease
(ichthyosis, agents for treatment of; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Skin, disease
(lentigines, agents for treatment of; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Analgesics
Anesthetics
(local; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Drug delivery systems
(lotions; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Skin, disease
(melasma, agents for treatment of; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Disease, animal
(mucous membrane, agents for treatment of; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Drug delivery systems
(ointments, creams; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)

IT Carboxylic acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(oxo; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Inflammation
Skin, disease
(pseudofolliculitis barbae, agents for treatment of; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Skin, disease
(rosacea, agents for treatment of; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Cosmetics
(skin-lightening; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Drug delivery systems
(solns.; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Drug interactions
(synergistic; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Foot
(toe, disease, corn, agents for treatment of; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT Cardiovascular agents
Drug delivery systems
(topical; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT 6949-98-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(Aleuritic acid; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT 594-61-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(Methyllactic acid; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT 56296-78-7, Fluoxetine hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(Prozac; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT 863910-51-4P
RL: COS (Cosmetic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)
IT 50-21-5, Lactic acid, reactions 76-93-7, Benzilic acid, reactions 77-92-9, Citric acid, reactions 77-95-2, Quinic acid 79-14-1, Glycolic acid, reactions 80-69-3, Tartronic acid 87-69-4, Tartaric acid, reactions 87-69-4D, oligomers 89-65-6, Isoascorbic acid 90-64-2, Mandelic acid 90-80-2, Gluconolactone 96-82-2, Lactobionic acid 109-52-4D, Pentanoic acid, stereoisomers, reactions 127-17-3, Pyruvic acid, reactions 133-37-9 147-24-0, Diphenhydramine hydrochloride 147-73-9, Erythraric acid 150-97-0, Mevalonic acid 156-06-9, Phenylpyruvic acid 298-12-4, Glyoxylic acid 300-85-6, 3-Hydroxybutanoic acid 320-77-4, Isocitric acid 328-51-8, 2-Ketooctanoic acid 473-81-4, Glyceric acid 488-31-3, Pentaric acid 503-66-2, 3-Hydroxypropanoic acid 515-30-0, Atrolactic acid 526-95-4, D-Gluconic acid 526-99-8, Galactaric acid 527-00-4, Allaric acid 527-03-7D, Heptaric acid, stereoisomers 534-41-8, Cellobionic acid 534-42-9, Maltobionic acid 534-74-7, Isomaltobionic acid 544-57-0, Cerebronic acid 552-63-6, Tropic acid 584-63-4 597-44-4, Citramalic acid 599-04-2, Pantolactone 600-15-7, 2-Hydroxybutanoic acid 600-18-0, 2-Ketobutanoic acid 611-73-4, Benzoylformic acid 617-31-2, 2-Hydroxypentanoic acid 617-57-2, Lactyl lactate 617-73-2, 2-Hydroxyoctanoic acid 636-69-1, 2-Hydroxyheptanoic acid 666-99-9, Agaricic acid 674-26-0, Mevalonolactone 685-73-4, Galacturonic acid 815-89-4, xylo-5-Hexulosonic acid 828-01-3, 3-Phenyllactic acid 1112-33-0, Pantoic acid 1310-73-2, Sodium hydroxide, reactions 1336-21-6, Ammonium hydroxide 1821-02-9, 2-Ketopentanoic acid

2492-75-3, 2-Ketohexanoic acid 2782-86-7D, Heptonic acid, stereoisomers 3063-04-5, Glucoheptonolactone 3327-64-8, Gulonolactone 3402-98-0, Iduronic acid 3646-68-2, Glucosaminic acid 3909-12-4, Threonic acid 3956-93-2, Idonic acid 5666-23-9, Altraric acid 5768-54-7, Idaric acid 5965-65-1, Lactobionolactone 6064-63-7, 2-Hydroxyhexanoic acid 6543-97-1, Mannaric acid 6556-12-3, Glucuronic acid 6703-05-5, Lyxaric acid 6708-50-5, Mannosaminic acid 6814-36-4, Mannuronic acid 6915-15-7, Malic acid 7270-86-2 7558-19-2D, Hexaric acid, stereoisomers 7760-07-8D, Hexonic acid, stereoisomers 10158-64-2, Xylaric acid 10191-35-2, 2,3,4-Trihydroxybutanoic acid 10237-77-1, 3-Hydroxypentanoic acid 13088-48-7, 2-Ketoheptanoic acid 13171-74-9, Pentonic acid 13382-27-9, Galactonic acid 13425-57-5, 5-Hexulosonic acid 13431-32-8, Laminaribionic acid 13752-84-6, Erythronic acid 15769-56-9, Guluronic acid 16533-48-5, xylo-2-Hexulosonic acid 16742-48-6, 2-Hydroxyeicosanoic acid 17812-24-7, Ribonic acid 17828-56-7, Xylonic acid 18404-70-1, Idonolactone 20246-52-0, Talonic acid 20246-53-1, Gulonic acid 20248-27-5, arabino-2-Hexulosonic acid 21675-38-7, Melibionic acid 22832-87-7, Miconazole nitrate 23351-51-1, Glucoheptonic acid 23593-75-1, Clotrimazole 24871-35-0, Altronic acid 25525-21-7, Glucaric acid 25596-90-1, Threonolactone 28060-81-3 28223-40-7, Lyxonic acid 28223-42-9, Allonic acid 28223-51-0, Alluronic acid 28223-52-1, Taluronic acid 28223-54-3, arabino-5-Hexulosonic acid 28223-56-5, ribo-5-Hexulosonic acid 28630-70-8 28630-71-9 28700-18-7, Galacturonolactone 30450-85-2 30923-19-4, Lyxuronic acid 30923-20-7, Riburonic acid 30923-21-8, Xyluronic acid 30923-39-8, Arabinuronic acid 32449-92-6, Glucuronolactone 33012-62-3, Ribaric acid 35388-57-9, Piscidic acid 36088-30-9D, stereoisomers 42776-28-3, Maltobionolactone 52762-22-8, Cellobionolactone 70803-53-1 73803-83-5, 2-keto-Gulonic acid 80490-57-9, 2-Ketododecanoic acid 81176-80-9, Galactosaminic acid 84710-55-4, Threuronic acid 84710-56-5, Erythruronic acid 84710-57-6, Altruronic acid 91698-32-7 122242-55-1D, stereoisomers 122242-56-2D, stereoisomers 214975-75-4, D-ribo-2-Hexulosonic acid 224785-91-5, Vardenafil hydrochloride 318471-21-5 318471-23-7 318471-25-9 318471-27-1 318471-28-2 318471-36-2 318471-37-3 318471-57-7 762262-34-0D, Hepturonic acid, stereoisomers 763103-38-4D, stereoisomers 763103-39-5 763103-40-8D, stereoisomers 763103-41-9 763103-42-0 763103-43-1 763103-44-2 763103-45-3 763103-47-5 763103-48-6D, stereoisomers 763103-49-7 763103-50-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)

IT 58-73-1DP, Diphenhydramine, gluconlactone/gluconic acid complexes 22916-47-8P, Miconazole 54910-89-3P, Fluoxetine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)

IT 50-44-2, Mercaptopurine 50-81-7, Ascorbic acid, biological studies 51-64-9, Dextroamphetamine 52-86-8, Haloperidol 57-92-1, Streptomycin, biological studies 58-00-4, Apomorphine 58-32-2, Dipyridamole 58-61-7, Adenosine, biological studies 58-93-5, Hydrochlorothiazide 70-51-9, Deferoxamine 73-48-3, Bendroflumethiazide 76-42-6, Oxycodone 77-86-1, Tromethamine 80-08-0, Dapsone 87-00-3, Homatropine 101-31-5, Hyoscyamine 104-31-4, Benzonatate 113-45-1, Methyl phenidate 127-69-5, Sulfisoxazole 147-94-4, Cytarabine 148-79-8, Thiabendazole 303-53-7, Cyclobenzaprine 357-70-0, Galantamine 446-86-6, Azathioprine 466-99-9, Hydromorphone 469-62-5, Propoxyphene 564-25-0, Doxycycline 657-24-9, Metformin 671-16-9, Procarbazine 723-46-6, Sulfamethoxazole 738-70-5, Trimethoprim 739-71-9, Trimipramine 911-45-5, **Clomiphene** 1744-22-5, Riluzole 2022-85-7, Flucytosine 2152-34-3, Pemoline 3313-26-6, Thiothixene 4291-63-8, Cladribine 4342-03-4, Dacarbazine 5633-20-5, Oxybutynin 6493-05-6, Pentoxifylline 13292-46-1, Rifampin 13392-28-4, Rimantadine 16679-58-6, Desmopressin 19387-91-8, Tinidazole 19982-08-2, Memantine 20594-83-6, Nalbuphine 20830-81-3, Daunorubicin 23214-92-8, Doxorubicin 24584-09-6, Dexrazoxane 27203-92-5, Tramadol 29975-16-4, Estazolam 31431-39-7, Mebendazole 32986-56-4, Tobramycin 34391-04-3, Levalbuterol 34580-13-7, Ketotifen 36791-04-5, Ribavirin 39809-25-1, Penciclovir

40431-64-9, Dexmethyl phenidate 42399-41-7, Diltiazem 42794-76-3, Midodrine 52485-79-7, Buprenorphine 53179-11-6, Loperamide 53714-56-0, Leuprolide 53910-25-1, Pentostatin 54063-53-5, Propafenone 54143-55-4, Flecainide 55096-26-9, Nalmefene 55985-32-5, Nicardipine 56420-45-2, Epirubicin 58581-89-8, Azelastine 58957-92-9, Idarubicin 59803-98-4, Brimonidine 61379-65-5, Rifapentine 63590-64-7, Terazosin 63675-72-9, Nisoldipine 65271-80-9, Mitoxantrone 66085-59-4, Nimodipine 66104-22-1, Pergolide 68475-42-3, Anagrelide 69655-05-6, Didanosine 70052-12-9, Eflornithine 72509-76-3, Felodipine 72599-27-0, Miglustat 73573-87-2, Formoterol 73590-58-6, Omeprazole 73963-72-1, Cilostazol 75847-73-3, Enalapril 76824-35-6, Famotidine 76963-41-2, Nizatidine 80621-81-4, Rifaximin 81103-11-9, Clarithromycin 81147-92-4, Esmolol 81403-80-7, Alfuzosin 81409-90-7, Cabergoline 82419-36-1, Ofloxacin 82626-48-0, Zolpidem 83015-26-3, Atomoxetine 83150-76-9, Octreotide 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 83905-01-5, Azithromycin 84625-61-6, Itraconazole 85441-61-8, Quinapril 85622-93-1, Temozolomide 85721-33-1, Ciprofloxacin 86386-73-4, Fluconazole 86541-75-5, Benazepril 87239-81-4, Cefpodoxime proxetil 88040-23-7, Cefepime 88150-42-9, Amlodipine 95058-81-4, Gemcitabine 97682-44-5, Irinotecan 100643-71-8, Desloratadine 100986-85-4, Levofloxacin 101828-21-1, Butenafine 103060-53-3, Daptomycin 103577-45-3, Lansoprazole 103775-14-0, Moexiprilat 104227-87-4, Famciclovir 106650-56-0, Sibutramine 107233-08-9, Cevimeline 107753-78-6, Zafirlukast 111025-46-8, Pioglitazone 112362-50-2, Dalfopristin 112809-51-5, Letrozole 112811-59-3, Gatifloxacin 113665-84-2, Clopidogrel 113806-05-6, Olopatadine 115103-54-3, Tiagabine 115256-11-6, Dofetilide 115956-12-2, Dolasetron 116539-59-4, Duloxetine 117467-28-4, Cefditoren pivoxil 119141-88-7, Esomeprazole 120014-06-4, Donepezil 120138-50-3, Quinupristin 120279-96-1, Dorzolamide 120511-73-1, Anastrozole 123441-03-2, Rivastigmine 124937-51-5, Tolterodine 128196-01-0, Escitalopram 129618-40-2, Nevirapine 129722-12-9, Aripiprazole 134678-17-4, Lamivudine 135729-61-2, Palonosetron 136470-78-5, Abacavir 136817-59-9, Delavirdine 137234-62-9, Voriconazole 139264-17-8, Zolmitriptan 139755-83-2, Sildenafil 142340-99-6, Adefovir dipivoxil 143322-58-1, Eletriptan 143491-57-0, Emtricitabine 144034-80-0, Rizatriptan 144494-65-5, Tirofiban 144689-63-4, Olmesartan medoxomil 144701-48-4, Telmisartan 145040-37-5, Candesartan cilexetil 145158-71-0, Tegaserod 150378-17-9, Indinavir 151096-09-2, Moxifloxacin 151319-34-5, Zaleplon 152459-95-5, Imatinib 154323-57-6, Almotriptan 159989-64-7, Nelfinavir 165800-03-3, Linezolid 169590-42-5, Celecoxib 170729-80-3, Aprepitant 171596-29-5, Tadalafil 175463-14-6, Gemifloxacin 184475-35-2, Gefitinib 188627-80-7, Eptifibatide 191114-48-4, Telithromycin 198904-31-3, Atazanavir 201341-05-1, Tenofovir disoproxil 224785-90-4, Vardenafil 226256-56-0, Cinacalcet
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)

IT 863910-49-0P 863910-50-3P 863910-52-5P 863910-53-6P 863913-34-2P 863913-35-3P 863913-36-4P 863913-49-9P 863913-50-2P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)

IT 57-55-6, Propylene glycol, biological studies 64-17-5, Ethanol, biological studies 110-63-4, Butylene glycol, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)

IT 50-02-2, Dexamethasone 50-03-3, Hydrocortisone 21-acetate 50-23-7, Hydrocortisone 50-28-2, Estradiol, biological studies 50-78-2, Acetylsalicylic acid 51-03-6, Piperonyl butoxide 51-21-8, 5-Fluorouracil 53-43-0, Dehydroepiandrosterone 53-86-1, Indomethacin 57-13-6, Urea, biological studies 57-63-6, Ethinyl estradiol 58-95-7, Vitamin E acetate 65-45-2, Salicylamide 67-73-2, Fluocinolone acetonide 67-78-7, Triamcinolone diacetate 68-26-8, Retinol 68-88-2, Hydroxyzine 69-72-7, Salicylic acid, biological studies 76-22-2,

Camphor 76-25-5, Triamcinolone acetonide 79-81-2, Retinyl palmitate 89-78-1, Menthol 93-60-7, Methyl nicotinate 94-36-0, Benzoyl peroxide, biological studies 103-16-2, Monobenzone 108-46-3, Resorcinol, biological studies 108-95-2, Phenol, biological studies 112-38-9, Undecylenic acid 116-31-4, Retinal 118-56-9, Homosalate 118-60-5, Octyl salicylate 119-36-8, Methyl salicylate 119-61-9, Benzophenone, biological studies 123-31-9, Hydroquinone, biological studies 123-31-9D, Hydroquinone, drivs. 123-99-9, Azelaic acid, biological studies 124-43-6, Carbamide peroxide 126-07-8, Griseofulvin 127-47-9, Retinyl acetate 131-57-7, Oxybenzone 136-77-6, Hexylresorcinol 137-66-6, Ascorbyl palmitate 139-12-8, Aluminum acetate 302-79-4, Retinoic acid 356-12-7, Fluocinonide 382-67-2, Desoximetasone 404-86-4, Capsaicin 501-30-4, Kojic acid 1143-38-0, Anthralin 1319-82-0, Aminocaproic acid 1321-11-5, Aminobenzoic acid 1321-23-9, Chloroxylenol 1327-41-9, Aluminum chlorohydroxide 1405-87-4, Bacitracin 1946-82-3, N-Acetyl-L-lysine 2152-44-5, Betamethasone valerate 3380-34-5, Triclosan 4759-48-2 5466-77-3, Octyl methoxycinnamate 5534-09-8, Beclomethasone dipropionate 5593-20-4, Betamethasone dipropionate 5611-51-8, Triamcinolone hexacetonide 6205-08-9, N-Acetylornithine 7446-70-0, Aluminum chloride, biological studies 7488-56-4, Selenium sulfide 7512-17-6, N-Acetylglucosamine 7704-34-9, Sulfur, biological studies 7722-84-1, Hydrogen peroxide, biological studies 9012-76-4, Chitosan 13463-41-7, Zinc pyrithione 13609-67-1, Hydrocortisone 17-butyrate 15687-27-1, Ibuprofen 16395-58-7, N-Acetylprolinamide 21245-02-3, Padimate O 21645-51-2, Aluminum hydroxide, biological studies 22204-53-1, Naproxen 25122-46-7, Clobetasol propionate 25655-41-8, Povidone iodine 28088-64-4, Aminosalicylic acid 29342-05-0, Ciclopirox 52645-53-1, Permethrin 57524-89-7, Hydrocortisone 17-valerate 66734-13-2, Aclovate 106685-40-9, Adapalene 112965-21-6, Calcipotriene
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination with; bioavailability and improved delivery of alkaline drugs by complexation with acids or lactones)

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ACCESSION NUMBER: 2005:509262 BIOSIS
DOCUMENT NUMBER: PREV200510298998
TITLE: International Congress Series.
AUTHOR(S): Slager, E [Editor]; Fauser, B [Editor]; VanGeijn, H [Editor]; Brolmann, H [Editor]; Vervest, H [Editor]
SOURCE: Slager, E [Editor]; Fauser, B [Editor]; VanGeijn, H [Editor]; Brolmann, H [Editor]; Vervest, H [Editor]. Int. Congr. Ser. - Excerpta Med., (2005) International Congress Series.
Publisher: ELSEVIER SCIENCE BV, SARA BURGERHARTSTRAAT 25, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS. Series: INTERNATIONAL CONGRESS SERIES.
CODEN: EXMDA4. ISSN: 0531-5131. ISBN: 0-444-51917-3(H).
DOCUMENT TYPE: Book
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Nov 2005
Last Updated on STN: 23 Nov 2005

AB This 476-page book, which is based on the proceedings of the Fifteenth Congress of Gynecology, Obstetrics and Reproductive Medicine, is volume 1279 of the International Congress Series and this volume focuses on gynecology, obstetricsand reproductive medicine in daily practice. The congress was held in Rotterdam, The Netherlands, in April 2005. The book is structured into 5 major sections, which in turn may be divided into more specific sections. There are 71 individually-authored papers in total, which include key note lectures. The text is in English and all of the papers are extensively-referenced. Fertility research and treatment in 2005 is the focus of the first section, which contains 11 papers, and topics discussed in the more specific subsections include anovulation diagnostics, ovulation induction, ovarian stimulation, and intrauterine insemination. Gynecology is the focus of the next major section and is discussed in terms of disease prevention, diagnostics and therapy in 2005. Specific subsections within this second section deal with chronic pelvic pain, infections, endometrial carcinoma, and new diagnostics and operating

techniques. The third major section deals with postgraduate course prenatal imaging and screening and specific areas outlined include the mid-gestational scan, ultrasound examination in twin pregnancies, nuchal translucency, first trimester ultrasound screening for chromosomal anomalies, a national screening program for Downs syndrome and neural tube defects in the Netherlands, Down syndrome screening, fetal aneuploidy screening practice in Flanders and Belgium, and prenatal screening and the communication and perception of risks. The next major section overviews obstetrics with respect to preconceptional, antenatal and perinatal prevention of morbidity and mortality in 2005, and more specific subsections discuss preconceptional counselling, antepartum fetal care, intrapartum fetal care,postpartum hemorrhage, and newborn life support. The final major section discusses postgraduate course vaginal prolapse and urine incontinence. The book isindexed by author and by keyword. This book will be of interest to gynecologists, urologists, obstetricians and anyone interested in reproductive medicine.

IT Major Concepts
Urology (Human Medicine, Medical Sciences); Obstetrics (Human Medicine, Medical Sciences); Gynecology (Human Medicine, Medical Sciences)

IT Parts, Structures, & Systems of Organisms
urine: excretory system; vagina: reproductive system; endometrium: reproductive system; amniotic fluid: embryonic structure; uterine artery: circulatory system; ovaries: reproductive system

IT Diseases
diabetes mellitus: endocrine disease/pancreas, metabolic disease
Diabetes Mellitus (MeSH)

IT Diseases
**HIV** infection: blood and lymphatic disease, immune system disease, viral disease, human immunodeficiency virus infection

IT Diseases
urinary incontinence: urologic disease
Urinary Incontinence (MeSH)

IT Diseases
intrauterine growth retardation: congenital disease
Fetal Growth Retardation (MeSH)

IT Diseases
postpartum hemorrhage: reproductive system disease/female
Postpartum Hemorrhage (MeSH)

IT Diseases
pre-eclampsia: vascular disease, reproductive system disease/female
Pre-Eclampsia (MeSH)

IT Diseases
polycystic ovary syndrome: reproductive system disease/female, endocrine disease/gonads
Polycystic Ovary Syndrome (MeSH)

IT Diseases
HELLP syndrome: reproductive system disease/female

IT Diseases
Down syndrome: nervous system disease, behavioral and mental disorders, congenital disease, diagnosis

IT Diseases
neural tube defect: nervous system disease, congenital disease, diagnosis
Neural Tube Defects (MeSH)

IT Diseases
hypoxic-ischemic encephalopathy: vascular disease, injury, nervous system disease
Hypoxia-Ischemia, Brain (MeSH)

IT Diseases
endometrial carcinoma: neoplastic disease, reproductive system disease/female, diagnosis, radiotherapy
Endometrial Neoplasms (MeSH); Carcinoma (MeSH)

IT Diseases
anovulation: reproductive system disease/female, endocrine disease/gonads, drug therapy, diagnosis
Anovulation (MeSH)

IT Diseases
chronic pelvic pain: nervous system disease, epidemiology
Pelvic Pain (MeSH)

IT Diseases
neonatal herpes infection: viral disease
IT Diseases
cytomegalovirus infection: congenital disease, viral disease, diagnosis
Cytomegalovirus Infections (MeSH)
IT Diseases
areobic vaginitis: bacterial disease, reproductive system disease/female
IT Diseases
uterine fibroids: reproductive system disease/female, surgery
IT Diseases
fetal aneuploidy: congenital disease, diagnosis
IT Diseases
vaginal prolapse: urologic disease, reproductive system disease/female
IT Chemicals & Biochemicals
gonadotropins: hormone-drug; insulin sensitizers: metabolic-drug; **clomiphene**: hormone-drug, contraceptive-drug
IT Methods & Equipment
prenatal diagnosis: clinical techniques, diagnostic techniques; radiotherapy: therapeutic and prophylactic techniques, clinical techniques; hysterectomy: therapeutic and prophylactic techniques, clinical techniques; ultrasound imaging: laboratory techniques, diagnostic techniques, clinical techniques, imaging and microscopy techniques; hormone replacement therapy: therapeutic and prophylactic techniques, clinical techniques; Doppler imaging: laboratory techniques, diagnostic techniques, clinical techniques, imaging and microscopy techniques; intrauterine insemination: clinical techniques; uterine artery embolization: therapeutic and prophylactic techniques, clinical techniques; ovarian stimulation: therapeutic and prophylactic techniques, clinical techniques; cancer immunotherapy: therapeutic and prophylactic techniques, clinical techniques; laparoscopic electrocautery: therapeutic and prophylactic techniques, clinical techniques; prenatal imaging: clinical techniques, diagnostic techniques; laparoscopic adhesiolysis: therapeutic and prophylactic techniques, clinical techniques; prepregnancy counseling: clinical techniques; **HIV** post-exposure prophylaxis: therapeutic and prophylactic techniques, clinical techniques; intravenous contrast ultrasound: clinical techniques, diagnostic techniques; mid-gestational scan: clinical techniques, diagnostic techniques
IT Miscellaneous Descriptors
occupational exposure; multiple pregnancy; risk perception; risk communication; twin pregnancy; fetal growth; ovulation; pregnancy rate; amniotic fluid volume; surgical staging; EMMY trial; preconception care; sexological issue; non-occupational exposure; teratogenic medication risks; uterine artery Doppler flow velocity; inatrapartum fetal care
GT USA (North America, Nearctic region); Europe (Palearctic region); Netherlands (Europe, Palearctic region); UK (Europe, Palearctic region); Belgium (Europe, Palearctic region); Greece (Europe, Palearctic region); Flanders (Belgium, Europe, Palearctic region)
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human (common): newborn, adult
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 911-45-5 (**clomiphene**)

L23 ANSWER 11 OF 160 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:440028 CAPLUS
DOCUMENT NUMBER: 143:206639
TITLE: Antral follicle count and FSH concentration after **clomiphene** citrate challenge test in the prediction of ovarian response during IVF treatment
AUTHOR(S): Ng, Ernest Hung Yu; Chan, Carina Chi Wai; Tang, Oi Shan; Ho, Pak Chung
CORPORATE SOURCE: Department of Obstetrics and Gynaecology, The

University of Hong Kong, Pokfulam Road, People's Republic of China, Hong Kong Special Administrative Region, Hong Kong, Peop. Rep. China
SOURCE: Human Reproduction (2005), 20(6), 1647-1654
CODEN: HUREEE; ISSN: 0268-1161
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors compared: (i) antral follicle count (AFC) in the early follicular phase, after the **clomiphene** citrate challenge test (CCCT) and before ovarian stimulation following pituitary down-regulation; and (ii) age of women, body mass index, basal and stimulated serum FSH concns. and AFC in predicting the ovarian response of infertile women aged <40 years with basal FSH <10 IU/l on recruitment in their first IVF cycle. Two months prior to the treatment cycle, AFC and basal FSH concentration were determined on day 2-3 of a spontaneous period and on day 10 after CCCT. All women received a standard stimulation regimen. Ovarian response was represented by the number of oocytes, serum estradiol, the duration and dosage of gonadotrophins. There was no significant difference between basal, stimulated and down-regulated AFC. AFC achieved the best predictive value in relation to the number of oocytes, followed by combined FSH concentration (sum of the two FSH concns.) and age of women. Both basal AFC and combined FSH concentration were predictive factors of serum estradiol concentration, whereas stimulated FSH concentration was predictive of the total dosage of gonadotrophins. Thus, combined FSH concentration after CCCT provides addnl. information in predicting ovarian response.
IT **Aging**, animal
Body weight
Fertility disorders
Human
In vitro fertilization
Oogenesis
Ovary
(antral follicle count and FSH concentration after **clomiphene** citrate challenge test in prediction of ovarian response during IVF treatment)
IT Ovarian cycle
(follicular phase; antral follicle count and FSH concentration after **clomiphene** citrate challenge test in prediction of ovarian response during IVF treatment)
IT Egg
(oocyte; antral follicle count and FSH concentration after **clomiphene** citrate challenge test in prediction of ovarian response during IVF treatment)
IT Ovary
(preovulatory follicle; antral follicle count and FSH concentration after **clomiphene** citrate challenge test in prediction of ovarian response during IVF treatment)
IT 50-28-2, Estradiol, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antral follicle count and FSH concentration after **clomiphene** citrate challenge test in prediction of ovarian response during IVF treatment)
IT 9002-68-0, FSH
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(antral follicle count and FSH concentration after **clomiphene** citrate challenge test in prediction of ovarian response during IVF treatment)
IT 50-41-9, **Clomid** 9002-61-3, Profasi 61489-71-2, Pergonal
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antral follicle count and FSH concentration after **clomiphene** citrate challenge test in prediction of ovarian response during IVF treatment)
REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

reserved on STN
ACCESSION NUMBER: 2005490819 EMBASE
TITLE: Selective estrogen receptor modulators (SERMs) for the brain: Current status and remaining challenges for developing NeuroSERMs.
AUTHOR: Zhao L.; O'Neill K.; Diaz Brinton R.
CORPORATE SOURCE: R. Diaz Brinton, Department of Molecular Pharmacology and Toxicology, School of Pharmacy, University of Southern California, Los Angeles, CA 90089, United States. rbrinton@hsc.usc.edu
SOURCE: Brain Research Reviews, (2005) Vol. 49, No. 3, pp. 472-493. .
Refs: 208
ISSN: 0165-0173 CODEN: BRERD2
PUBLISHER IDENT.: S 0165-0173(05)00024-X
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20051201
Last Updated on STN: 20051201

AB Multiple issues regarding the efficacy of estrogen action in the brain remain unresolved. These include the timing, formulation and duration of the therapy intervention. Moreover, issues of thrombotic and neoplastic risks must be factored into the design of estrogen alternatives developed to prevent age-associated neurodegenerative disorders, as well as other climacteric symptoms such as hot flush and sleep dysfunction. One strategy to address these issues is to develop molecules that selectively target and activate estrogen mechanisms of action in the brain while avoiding activation of estrogen receptors peripheral to the brain, particularly in reproductive organs. An overview of recent advances in our understanding of the molecular mechanisms of estrogen action is discussed in the context of designing an efficacious NeuroSERM that will activate cellular, biochemical and genomic events required for the promotion of memory function and neuronal survival. Pharmacological analyses of estrogen receptor subtypes and the case for a membrane-associated estrogen receptor splice variant in mediating these mechanisms are provided along with a summary of the activation profiles of existing clinically relevant estrogen alternatives or SERMs in neurons. Results of these endeavors have yielded insights into strategies for developing novel molecules with NeuroSERM potential in order to prevent brain related climacteric symptoms and neurodegenerative diseases.


L23 ANSWER 13 OF 160 EMBASE 
ACCESSION NUMBER: 2005379947 EMBASE
TITLE: Ovarian reserve.
AUTHOR: Macklon N.S.; Fauser B.C.J.M.
CORPORATE SOURCE: Dr. N.S. Macklon, Department of Gynecology and Reproductive Medicine, University Medical Centre, Utrecht, Heidelberglaan 100, 3584 CX Utrecht, Netherlands. n.macklon@umcutrecht
SOURCE: Seminars in Reproductive Medicine, (2005) Vol. 23, No. 3, pp. 248-256. .
Refs: 78
ISSN: 1526-8004 CODEN: SRMECJ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 010 Obstetrics and Gynecology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20050922
Last Updated on STN: 20050922

AB The tendency to delay childbirth has increased the importance of ovarian reserve as a determinant of infertility treatment outcome. In the context of assisted reproduction technology, effective strategies to overcome the impact of ovarian **aging** and diminished ovarian reserve on pregnancy chances remain elusive. Markers of ovarian reserve are increasingly used to aid management and counseling of these patients. Proper interpretation of currently applied hormonal markers, ultrasound parameters, and hormone challenge tests requires an understanding of what constitutes and determines ovarian reserve. This article addresses these aspects and highlights recent developments in the field. Copyright .COPYRGT. 2005 by Thieme Medical Publishers, Inc.

L23 ANSWER 14 OF 160 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2005396341 EMBASE
TITLE: Pharmacology of estrogens and progestogens: Influence of different routes of administration.
AUTHOR: Kuhl H.
CORPORATE SOURCE: Prof. H. Kuhl, Department of Obstetrics, J. W. Goethe University, Theodor-Stern-Kai 7, D-60590 Frankfurt am Main, Germany
SOURCE: Climacteric, (2005) Vol. 8, No. SUPPL. 1, pp. 3-63. .
Refs: 333
ISSN: 1369-7137 CODEN: CLIMFC
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20051006
Last Updated on STN: 20051006

AB This review comprises the pharmacokinetics and pharmacodynamics of natural and synthetic estrogens and progestogens used in contraception and therapy, with special consideration of hormone replacement therapy. The paper describes the mechanisms of action, the relation between structure and hormonal activity, differences in hormonal pattern and potency, peculiarities in the properties of certain steroids, tissue-specific effects, and the metabolism of the available estrogens and progestogens. The influence of the route of administration on pharmacokinetics, hormonal activity and metabolism is presented, and the effects of oral and transdermal treatment with estrogens on tissues, clinical and serum parameters are compared. The effects of oral, transdermal (patch and gel), intranasal, sublingual, buccal, vaginal, subcutaneous and intramuscular administration of estrogens, as well as of oral, vaginal, transdermal, intranasal, buccal, intramuscular and intrauterine application of progestogens are discussed. The various types of progestogens, their receptor interaction, hormonal pattern and the hormonal activity of certain metabolites are described in detail. The structural formulae, serum concentrations, binding affinities to steroid receptors and serum binding globulins, and the relative potencies of the available estrogens and progestins are presented. Differences in the tissue-specific effects of the various compounds and regimens and their potential implications with the risks and benefits of hormone replacement therapy are discussed. .COPYRGT. 2005 International Menopause Society.

L23 ANSWER 15 OF 160 CAPLUS COPYRIGHT 2006 ACS on STN

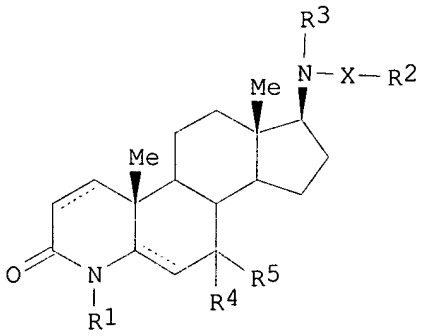
ACCESSION NUMBER: 2004:1015853 CAPLUS
DOCUMENT NUMBER: 142:1359
TITLE: Identification and synthesis of androgen receptor modulators and therapeutic uses thereof
INVENTOR(S): Meissner, Robert S.; Perkins, James J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 165 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004100874 | A2 | 20041125 | WO 2004-US13787 | 20040503 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2524409 | AA | 20041125 | CA 2004-2524409 | 20040503 |
| EP 1622567 | A2 | 20060208 | EP 2004-751257 | 20040503 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR | | | | |

PRIORITY APPLN. INFO.: US 2003-468579P P 20030507
WO 2004-US13787 W 20040503

OTHER SOURCE(S): MARPAT 142:1359
GI




I

AB Compds. of structural formula (I) as herein defined are disclosed as useful in a method for modulating the androgen receptor in a tissue selective manner in a patient in need of such modulation, as well as in a method of agonizing the androgen receptor in a patient, and in particular the method wherein the androgen receptor is antagonized in the prostate of a male patient or in the uterus of a female patient and agonized in bone and/or muscle tissue. Method for the synthesis of those compds., as well as techniques for the screening of androgen receptor modulation capacity of those compds. are exemplified. These compds. are useful in the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including: osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, **aging** skin, male hypogonadism, post-menopausal symptoms in women, female sexual dysfunction, atherosclerosis, hypercholesterolemia, hyperlipidemia, aplastic anemia and other hematopoietic disorders, pancreatic cancer, renal cancer, arthritis and joint repair, alone or in combination with other active agents. In addition, these compds. are useful as pharmaceutical composition ingredients alone and in combination with other active agents.

IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(2, further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)

IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(3, further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(5, further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(6, further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Bone morphogenetic proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(7, further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Acid halides
RL: RCT (Reactant); RACT (Reactant or reagent)
(acid chlorides; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Skin, disease
(**aging**; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Prostacyclin receptors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(agonist, further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Androgens
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(agonists and antagonists; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Bone
Muscle
(androgen agonism in; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Prostate gland
Uterus
(androgen antagonism in; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Antiarthritics
Anticholesteremic agents
Antitumor agents
Bone resorption inhibitors
Hypolipemic agents
(androgen receptor modulators as; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Antiarteriosclerotics
(antiatherosclerotics, androgen receptor modulators as; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Anemia (disease)
(aplastic; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Osteoclast
(binding of VEGF to, inhibitor of, further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)

IT Injury
(bone, following bone reconstructive surgery; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Receptors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(calcium, antagonist, further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT **Cachexia**
(cancerous; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Estrogens
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugated, further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Prostaglandins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(derivs., further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Ovary, disease
(failure, premature; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Sexual disorders
(female; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Drug screening
(for androgen receptor modulators; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Bone, disease
(fracture; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Selective estrogen receptor modulators
(further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Antiestrogens
Bone morphogenetic proteins
Estrogens
Progestogens
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hyperlipidemia; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Testis, disease
(hypogonadism; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Arthritis
Atherosclerosis
Autoimmune disease
Hematopoietic disorders
Human
Hypercholesterolemia
Kidney, neoplasm
Muscular dystrophy
Osteoporosis
Pancreas, neoplasm
Periodontium, disease
(identification and synthesis of androgen receptor modulators and therapeutic uses thereof)

IT Androgen receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Antiandrogens
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Amines, reactions
Isocyanates
RL: RCT (Reactant); RACT (Reactant or reagent)
(identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Drug delivery systems
(injections; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Bone, disease
(injury, following bone reconstructive surgery; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Integrins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(osteoclast, inhibitor, further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Bone, disease
(osteopenia; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Menopause
(postmenopause, -associated symptoms; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Joint, anatomical
(repair; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Androgens
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(replacement therapy; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Muscle
(sarcopenia; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Bone formation
(stimulation by androgen receptor modulators; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Diet
(supplements, calcium, further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Drug delivery systems
(suppositories; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Drug delivery systems
(transdermal; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Prostanoid receptors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type EP1, agonist, further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)
IT Prostanoid receptors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type EP2, agonist, further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators

and therapeutic uses thereof)

IT Prostanoid receptors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type EP4, agonist, further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)

IT Prostanoid receptors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(type FP, agonist, further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)

IT Disease, animal
(wasting, **HIV**-induced; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)

IT Integrins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(αvβ3, inhibitor, further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)

IT Integrins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(αvβ5, inhibitor, further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)

IT Transforming growth factors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β-, further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)

IT Peroxisome proliferator-activated receptors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(γ, further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)

IT 13598-36-2D, Phosphonic acid, alkylidenebis- derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Bisphosphonate, further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)

IT 127464-60-2, Vascular endothelial growth factor
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(binding to osteoclast receptors, inhibitor of, further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)

IT 7440-70-2, Calcium, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(from dietary supplements, further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)

IT 50-28-2, Estradiol, biological studies 53-16-7, Estrone, biological studies 67-96-9, Dihydrotachysterol 67-98-1, Mer-25 68-22-4, Norethindrone 71-58-9, Medroxyprogesterone acetate 471-34-1, Calcium carbonate, biological studies 911-45-5, **Clomiphene** 1406-16-2, Vitamin D 1406-16-2D, Vitamin D, derivs. 1845-11-0, Nafoxidine 2809-21-4 4717-38-8, 17β-Ethynyl estradiol 5863-35-4, CI-628 7440-70-2D, Calcium, salts 7681-49-4, Sodium fluoride, biological studies 7693-13-2, Calcium citrate 9002-64-6, Parathyroid hormone 9007-12-9, Calcitonin 10540-29-1, Tamoxifen 10596-23-3 12001-79-5, Vitamin K 12001-79-5D, Vitamin K, derivs. 15690-55-8, Zuclomiphene 15690-57-0, **Enclomiphene**

16984-48-8D, Fluoride, salts 19356-17-3, 25-Hydroxy-vitamin D3
20859-36-3, Monosodium fluorophosphate 32222-06-3, 1α,25-Dihydroxy
vitamin D3 35212-22-7, Ipriflavone 40391-99-9, 3-Amino-1-
hydroxypropylidene-1,1-bisphosphonic acid 41294-56-8 47931-85-1,
Salmon calcitonin 50948-44-2, U-11, biological studies 52232-67-4,
1-34-Parathormone (human) 54573-75-0 56287-31-1, CI-680 57333-95-6
57333-96-7 61912-98-9, Insulin-like growth factor 63132-39-8
66376-36-1, 4-Amino-1-hydroxybutylidene-1,1-bisphosphonic acid
67763-96-6, IGF I 67763-97-7, IGF II 68893-82-3, 1-84-Parathormone
(human) 75330-75-5, Lovastatin 78994-23-7, Levormeloxifene
79778-41-9 79902-63-9, Simvastatin 81093-37-0, Pravastatin
82413-20-5, Droloxifene 83805-11-2 84449-90-1, Raloxifene
89778-26-7, Toremifene 93957-54-1, Fluvastatin 103909-75-7,
22-Oxacalcitriol 104121-92-8, ED71 104361-73-1 105462-24-6
106096-92-8, AFGF 106096-93-9, Basic fibroblast growth factor
112965-21-6, Calcipotriol 116057-75-1, Idoxifene 116162-22-2
118072-93-8 118694-43-2, Ro 23-7553 121009-77-6 129318-43-0,
4-Amino-1-hydroxybutylidene-1,1-bisphosphonic acid monosodium salt
130447-37-9, 19-Nor-1α,25-dihydroxy vitamin D3 131875-08-6, KH1060
134399-24-9 134404-52-7, EB1089 134523-00-5, Atorvastatin
134523-84-5 141750-63-2, Nisvastatin 145599-86-6, Cerivastatin
147511-69-1, Pitavastatin 180064-38-4 180916-16-9, Lasofoxifene
182133-25-1, Arzoxifene 182167-02-8, EM-652 182167-03-9, EM-800
193830-08-9, GDF5 198481-33-3, TSE 424 287714-41-4, Rosuvastatin
304853-26-7, Growth hormone, secretagogue 530109-46-7,
1-Hydroxy-3-(N-methyl-N-pentylamino)propylidene-1,1-bisphosphonic acid
583063-07-4, 1-84-Parathormone (human) 797050-64-7, 555A 797050-81-8,
U 100A
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(further administered with androgen modulator treatment; identification
and synthesis of androgen receptor modulators and therapeutic uses
thereof)

IT 796884-38-3P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic
preparation); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); RACT (Reactant or reagent); USES (Uses)
(identification and synthesis of androgen receptor modulators and
therapeutic uses thereof)

IT 154112-31-9P 154112-38-6P 154112-39-7P 154112-41-1P 154112-55-7P
154112-61-5P 154112-62-6P 154112-63-7P 154112-66-0P 154112-67-1P
154112-69-3P 796884-39-4P 796884-40-7P 796884-41-8P 796884-42-9P
796884-43-0P 796884-44-1P 796884-45-2P 796884-46-3P 796884-47-4P
796884-48-5P 796884-49-6P 796884-50-9P 796884-51-0P 796884-52-1P
796884-53-2P 796884-54-3P 796884-55-4P 796884-56-5P 796884-57-6P
796884-58-7P 796884-59-8P 796884-60-1P 796884-61-2P 796884-62-3P
796884-63-4P 796884-64-5P 796884-65-6P 796884-66-7P 796884-67-8P
796884-68-9P 796884-69-0P 796884-70-3P 796884-71-4P 796884-72-5P
796884-73-6P 796884-74-7P 796884-75-8P 796884-76-9P 796884-77-0P
796884-78-1P 796884-79-2P 796884-80-5P 796884-81-6P 796884-82-7P
796884-83-8P 796884-84-9P 796884-85-0P 796884-86-1P 796884-87-2P
796884-88-3P 796884-89-4P 796884-90-7P 796884-91-8P 796884-92-9P
796884-93-0P 796884-94-1P 796884-95-2P 796884-96-3P 796884-97-4P
796884-98-5P 796884-99-6P 796885-00-2P 796885-01-3P 796885-03-5P
796885-04-6P 796885-06-8P 796885-07-9P 796885-08-0P 796885-10-4P
796885-12-6P 796885-14-8P 796885-16-0P 796885-18-2P 796885-20-6P
796885-23-9P 796885-25-1P 796885-27-3P 796885-29-5P 796885-31-9P
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796885-42-2P 796885-43-3P 796885-44-4P 796885-45-5P 796885-46-6P
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796885-52-4P 796885-53-5P 796885-54-6P 796885-55-7P 796885-56-8P
796885-57-9P 796885-58-0P 796885-59-1P 796885-60-4P 796885-61-5P
796885-62-6P 796885-63-7P 796885-64-8P 796885-65-9P 796885-66-0P
796885-67-1P 796885-68-2P 796885-69-3P 796885-70-6P 796885-71-7P
796885-72-8P 796885-73-9P 796885-74-0P 796885-75-1P 796885-76-2P
796885-77-3P 796885-78-4P 796885-79-5P 796885-80-8P 796885-81-9P
796885-82-0P 796885-83-1P 796885-84-2P 796885-85-3P 796885-86-4P
796885-87-5P 796885-88-6P 796885-89-7P 796885-90-0P 796885-91-1P

796885-92-2P 796885-93-3P 796885-94-4P 796885-95-5P 796885-96-6P
796885-97-7P 796885-98-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(identification and synthesis of androgen receptor modulators and therapeutic uses thereof)

IT 98-09-9, Phenylsulfonyl chloride 103-71-9, Phenyl isocyanate, reactions 121-44-8, Triethylamine, reactions 312-94-7, 2-Trifluoromethylbenzoyl chloride 593-51-1, Methylamine hydrochloride 661-20-1, Isocyanate 1885-14-9, Phenyl chloroformate 7087-68-5, Diisopropylethylamine 7791-25-5D, Sulfonyl chloride, derivs. 26386-88-9, Diphenylphosphoryl azide 26628-22-8, Sodium azide 96692-02-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(identification and synthesis of androgen receptor modulators and therapeutic uses thereof)

IT 9028-35-7, HMG-CoA reductase 94716-09-3, Cathepsin K 165245-96-5, p38 Kinase
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor, further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)

IT 9000-83-3, ATPase
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(osteoclast vacuolar, inhibitor, further administered with androgen modulator treatment; identification and synthesis of androgen receptor modulators and therapeutic uses thereof)

L23 ANSWER 16 OF 160 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:995989 CAPLUS
DOCUMENT NUMBER: 142:747
TITLE: Combination treatment with strontium for the prophylaxis and/or treatment of cartilage and/or bone conditions
INVENTOR(S): Hansen, Christian; Nilsson, Henrik
PATENT ASSIGNEE(S): Nordic Bone A/S, Den.; Osteologix A/S; Christgau, Stephan
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004098618 | A2 | 20041118 | WO 2004-DK327 | 20040506 |
| WO 2004098618 | A3 | 20050324 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2524610 | AA | 20041118 | CA 2004-2524610 | 20040506 |
| EP 1622630 | A2 | 20060208 | EP 2004-731315 | 20040506 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| WO 2005108339 | A2 | 20051117 | WO 2005-DK307 | 20050505 |
| WO 2005108339 | A3 | 20051229 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, | | | | |

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,
SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,
ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| DK 2003-691 | A | 20030507 |
| DK 2003-931 | A | 20030620 |
| DK 2003-1819 | A | 20031209 |
| US 2003-528548P | P | 20031209 |
| WO 2004-DK326 | A | 20040506 |
| WO 2004-DK327 | W | 20040506 |
| WO 2004-DK328 | A | 20040506 |
| DK 2004-1708 | A | 20041105 |


AB A combination treatment, wherein a strontium-containing compound together with one or more active substances capable of reducing the incidence of bone fracture and/or increasing bone d. and/or improving healing of fractured bone and/or improving bone quality are administered for use in the treatment and/or prophylaxis of cartilage and/or bone conditions.

IT Disease, animal
(Bechet's disease; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)

IT Bone, disease
(Paget's; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)

IT Drug interactions
(additive; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)

IT Development, mammalian postnatal
(adolescent; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)

IT Bone minerals
(bone mineral d. (BMD), bone mineral, d.; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)

IT Pain
(bone; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)

IT Development, mammalian postnatal
(child; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)

IT Antirheumatic agents
Antitumor agents
Bone, disease
Bone resorption
Bone resorption inhibitors
Cartilage
Combination chemotherapy
Drug bioavailability
Drug delivery systems
Human
Hyperparathyroidism
**Myositis**
Neoplasm
Osteoarthritis
Osteomalacia
Osteoporosis
Pharmacokinetics
Prophylaxis
Rheumatoid arthritis
(combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)

IT Steroids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(combination treatment with strontium for prophylaxis and/or treatment

of cartilage and/or bone conditions)
IT Glycosides
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coumarin; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Biological transport
(drug; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Intestine
(duodenum; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Bone, disease
(fracture; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Body weight
(gain; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Bone, disease
(hyperostosis; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Intestine
(jejunum; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Development, mammalian postnatal
(juvenile, osteoporosis; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Bone, neoplasm
(metastasis; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Antiarthritics
(osteoarthritis; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Bone, disease
(osteodystrophy; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Bone, disease
(osteolysis; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Bone, disease
(osteopenia; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Bone, disease
(osteopetrosis; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Eye, disease
Osteoporosis
(osteoporosis-pseudoglioma syndrome; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Inflammation
Periodontium, disease
(periodontitis; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Intestine
(small; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Inflammation
Spinal column, disease
(spondylitis, Bechterew's disease; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Sulfonic acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(strontium salts; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Drug interactions
(synergistic; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)

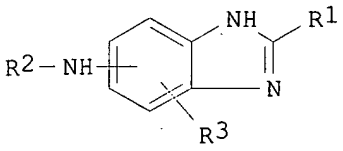
IT Drug delivery systems
(tablets, coated; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT 13598-36-2D, Phosphonic acid, alkylidenebis- derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Bisphosphonate; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT 182133-25-1, Arzoxifene
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LY-353381; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT 813-97-8P 868-19-9P 41839-80-9P 303730-87-2P 796104-86-4P 796842-36-9P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT 814-95-9 1633-05-2, Strontium carbonate 7759-02-6, Strontium sulfate 14332-40-2
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT 50-14-6, Vitamin D2 56-53-1 67-97-0, Vitamin D3 67-98-1, Ethamoxytriphetol 446-72-0, Genistein 493-08-3D, Chroman, derivs. 526-26-1 553-39-9, Allenolic acid 569-57-3, Chlorotrianisene 592-89-2, Strontium formate 911-45-5, **Clomiphene** 1845-11-0, Nafoxidine 2188-25-2 2624-43-3, Cyclophenyl 2809-21-4 5630-53-5, Tibolone 5863-35-4, Nitromifene citrate 7440-24-6D, Strontium, salts 7446-28-8, Strontium phosphate 7783-48-4, Strontium fluoride 9002-64-6, Parathyroid hormone 10042-76-9, Strontium nitrate 10101-21-0 10476-81-0, Strontium bromide 10476-85-4, Strontium chloride 10476-86-5, Strontium iodide 10540-29-1, Tamoxifen 10596-23-3 13451-02-0, Strontium sulfite 13470-06-9, Strontium nitrite 13703-84-9, Strontium borate 16067-69-9 16088-89-4 18808-42-9 19657-12-6 23287-50-5 27540-07-4 29870-99-3 31477-60-8, Ormeloxifene 34816-55-2, Moxestrol 40302-04-3 40391-99-9 40472-00-2 58429-84-8 60884-91-5 63524-05-0 66376-36-1, Alendronate 68047-06-3, 4-Hydroxy-tamoxifen 71912-45-3 77599-17-8, Panomifene 78994-23-7, Levormeloxifene 82413-20-5, Droloxifene 84449-90-1, Raloxifene 85169-08-0 86111-26-4, Zindoxifene 89778-26-7, Toremifene 89987-06-4, Tiludronate 98007-99-9 98774-23-3, Tesmilifene 103735-76-8, erythro-MEA 105462-24-6 114084-78-5, Ibandronate 115767-74-3, TAT-59 116057-68-2 116057-75-1, Idoxifene 118072-93-8, Zoledronate 124027-29-8 128607-22-7 129453-61-8, ICI 182780 129612-87-9, Miproxifene 135459-87-9, Strontium ranelate 165536-41-4, MDL-103323 180916-16-9, Lasofoxifene 182167-03-9, EM-800 190791-29-8, CP-336156 198481-32-2, Bazedoxifene 278172-05-7 452304-88-0 507471-56-9 796104-84-2 796104-90-0 796104-92-2 796104-97-7 796842-37-0 796842-38-1 796963-94-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT 10025-70-4P, Strontium chloride hexahydrate 120312-20-1P 127357-26-0P 796104-83-1P 796104-87-5P 796104-88-6P 796104-89-7P 796104-91-1P 796104-93-3P 796104-96-6P 796104-99-9P 796105-01-6P 796105-12-9P 796105-15-2P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT 7440-70-2, Calcium, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hypercalcemia; combination treatment with strontium for prophylaxis

and/or treatment of cartilage and/or bone conditions)

L23 ANSWER 17 OF 160 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:412812 CAPLUS
DOCUMENT NUMBER: 140:406808
TITLE: Preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators
INVENTOR(S): Kim, Yuntae; Spencer, Keith L.; Hanney, Barbara; Duggan, Mark E.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 136 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004041277 | A1 | 20040521 | WO 2003-US34345 | 20031028 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2504044 | AA | 20040521 | CA 2003-2504044 | 20031028 |
| EP 1581217 | A1 | 20051005 | EP 2003-777969 | 20031028 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| US 2006036098 | A1 | 20060216 | US 2005-533259 | 20050429 |
| PRIORITY APPLN. INFO.: | | | US 2002-422914P P | 20021101 |
| | | | WO 2003-US34345 W | 20031028 |

OTHER SOURCE(S): MARPAT 140:406808
GI

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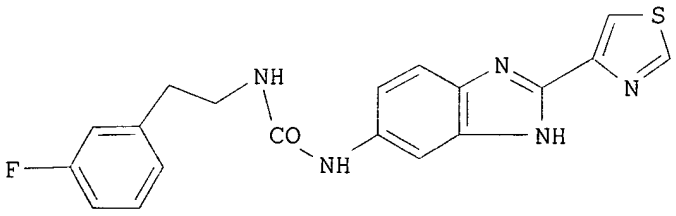


II

AB Carbonylamino-benzimidazoles (shown as I; variables defined below; e.g. II) are modulators of the androgen receptor (AR) in a tissue selective manner. They are useful as agonists of the androgen receptor in bone and/or muscle tissue while antagonizing the AR in the prostate of a male patient or in the uterus of a female patient. These compds. are therefore useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture,

bone damage following bone reconstructive surgery, sarcopenia, frailty, **aging** skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, arthritic condition and joint repair, **HIV**-wasting, prostate cancer, cancer **cachexia**, Alzheimer's disease, muscular dystrophies, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents. Although the methods of preparation are not claimed, 6 example prepns. and characterization data for .apprx.150 examples of I are included; nearly all examples contain the thiazol-4-yl group at the 2 position of the benzimidazole. For example, II was prepared from 3-fluorophenethylamine, 1,1'-carbonyldiimidazole and [2-(thiazol-4-yl)-3H-benzimidazol-5-yl]amine, the latter of which was prepared from thiazole-4-carboxylic acid and (4-amino-3-nitrophenyl)carbamic acid tert-Bu ester (preparation described) via amide formation followed by cyclization in 20% aqueous AcOH. For I: R1 = aryl or heterocyclyl; R2 = -(C:O)NR5R6, -(C:O)a(C1-10)alkyl, -(C:O)a(C2-8)alkenyl, -(C:O)a(C2-8)alkynyl, -(C:O)a(C3-10)cycloalkyl, -(C:O)a(C3-8)heterocyclyl, and -(C:O)aaryl; R3 = H, halogen, -(C:O)aOb(C1-10)alkyl, -(C:O)aOb(C2-8)alkenyl, -(C:O)aOb(C2-8)alkynyl, -(C:O)aOb(C3-10)cycloalkyl, -(C:O)aOb(C3-8)heterocyclyl, -(C:O)aObaryl, -(C:O)aNR5R6, -Ob(C:O)NR5R6, -NR5(C:O)aObRb, -NR5(C:O)NR5R6, -NR5S(O)2Rb, -(C:O)OH, trifluoromethoxy, trifluoroethoxy, -Ob(C1-10)perfluoroalkyl, -S(O)2Ob(C1-10)alkyl, -S(O)2Ob(C2-8)alkenyl, -S(O)2Ob(C2-8)alkynyl, -S(O)2Ob(C3-10)cycloalkyl, -S(O)2Ob(C3-8)heterocyclyl, -S(O)2Obaryl, -NR5S(O)2NR5R6, -CN, -NO2, oxo, and -OH; a = 0-1; b = 0-1; addnl. details are given in the claims.

IT Bone morphogenetic proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(2, codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Bone morphogenetic proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(3, codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Bone morphogenetic proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(5, codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Bone morphogenetic proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(6, codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Bone morphogenetic proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(7, codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Insulin-like growth factor-binding proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(IGFBP-3, codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Skin, disease
(**aging**; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Prostacyclin receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonists, codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Estrogens
Progestogens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(and derivs., codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Antiarteriosclerotics
(antiatherosclerotics; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Anemia (disease)
(aplastic; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(calcium, antagonists, codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT **Cachexia**
(cancerous; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Selective estrogen receptor modulators
(codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Antiestrogens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Bone morphogenetic proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Prostaglandins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Bone, disease
(damage following bone reconstructive surgery; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT X-ray spectroscopy
(dual-energy, method of effecting bone turnover marker using; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Bone, disease
(fracture; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Bone, disease
(frailty; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hyperlipidemia; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Reproductive system, disease
(hypogonadism, male; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Bone morphogenetic proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor of BMP antagonism, codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Bone minerals
(method for increasing d.; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Bone minerals
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(method for increasing d.; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Biomarkers
(method of effecting bone turnover marker; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Bone
(method of effecting turnover maker; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(osteoclast, antagonists of VEGF binding, codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Bone, disease
(osteopenia; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Menopause
(postmenopause, symptoms in women; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Ovary, disease
(premature ovarian failure; preparation of carbonylamino-benzimidazoles as

selective androgen receptor modulators)
IT Alzheimer's disease
Anti-**AIDS** agents
Anti-Alzheimer's agents
Antiarthritics
Anticholesteremic agents
Antiobesity agents
Antirheumatic agents
Antitumor agents
Arthritis
Atherosclerosis
Autoimmune disease
Bone resorption inhibitors
Drug delivery systems
Hematopoietic disorders
Human
Hypercholesterolemia
Hypolipemic agents
Immunomodulators
Muscular dystrophy
Obesity
Osteoarthritis
Osteoporosis
Periodontium, disease
Prostate gland, neoplasm
Rheumatoid arthritis
(preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)
IT Fluorides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(salts, codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)
IT Muscle, disease
(sarcopenia; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)
IT Androgen receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(selective modulators; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)
IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type EP1, agonists, codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)
IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type EP2, agonists, codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)
IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type EP4, agonists, codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)
IT Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(type FP, agonists, codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)
IT Collagens, analysis
RL: ANT (Analyte); ANST (Analytical study)
(type I, C-telopeptide, bone turnover marker; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)
IT Collagens, analysis
RL: ANT (Analyte); ANST (Analytical study)
(type I, N-telopeptide, bone turnover marker; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)
IT **AIDS** (disease)
(wasting; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)
IT Muscle, disease
(weakened muscle tone; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(αvβ3, antagonists, codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)
IT Transforming growth factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β-, codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)
IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(γ, activators, codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)
IT 13598-36-2D, Phosphonic acid, alkylidenebis- derivs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Bisphosphonate, codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)
IT 9002-64-6, Parathyroid hormone
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(and analogs, codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)
IT 9002-72-6, Growth hormone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(and secretagogues, codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)
IT 50-28-2, 17β-Estradiol, biological studies 53-16-7, Estrone, biological studies 64-96-0 67-96-9, Dihydrotachysterol 67-98-1, Mer-25 68-22-4, Norethindrone 71-58-9, Medroxyprogesterone acetate 471-34-1, Calcium carbonate, biological studies 911-45-5, **Clomiphene** 1845-11-0, Nafoxidene 2809-21-4 4717-38-8, 17β-Ethynyl estradiol 5863-35-4, CI-628 7681-49-4, Sodium fluoride, biological studies 7693-13-2, Calcium citrate 10540-29-1, Tamoxifen 10596-23-3 15690-55-8, Zuclomiphene 15690-57-0, **Enclomiphene** 19356-17-3, 25-OH vitamin D3 20859-36-3, Monosodium fluorophosphate 32222-06-3 35212-22-7, Ipriflavone 40391-99-9 41294-56-8 52232-67-4, Human parathyroid hormone(1-34) 54573-75-0 56287-31-1, CI-680 57333-95-6 57333-96-7 61912-98-9, Insulin-like growth factor 66376-36-1, Alendronate 68893-82-3, Human parathyroid hormone(1-84) 75330-75-5, Lovastatin 75755-07-6 78994-23-7, Levormeloxifene 79902-63-9, Simvastatin 80729-80-2 81093-37-0, Pravastatin 82413-20-5, Droloxifene 83805-11-2, 26,27-F6-1α,25(OH)2 vitamin D3 84449-90-1, Raloxifene 89778-26-7, Toremifene 89987-06-4 93957-54-1, Fluvastatin 103909-75-7, 22-Oxacalcitriol 104121-92-8, ED71 105462-24-6 106096-92-8, Acidic fibroblast growth factor 106096-93-9, Basic fibroblast growth factor 112965-21-6, Calcipotriol 114084-78-5, Ibandronate 116057-75-1, Idoxifene 118072-93-8, Zoledronate 118694-43-2, 1α,25(OH)2-16-ene-23-yne-vitamin D3 121009-77-6 121368-58-9, Olpadronate 129318-43-0, Monosodium alendronate 130447-37-9, 19-Nor-1α,25(OH)2 vitamin D3 131875-08-6, KH1060 134404-52-7, EB1089 134523-00-5, Atorvastatin 134523-84-5, 20-Epi-1α,25(OH)2 vitamin D3 138330-18-4, Incadronate 141750-63-2, Nisvastatin 145599-86-6, Cerivastatin 147511-69-1, Pitavastatin 180064-38-4 180916-16-9, Lasofoxifene 182133-25-1, Arzoxifene 182167-02-8, EM-652 182167-03-9, EM-800 198481-33-3, TSE 424 205944-50-9, Osteoprotegerin 287714-41-4, Rosuvastatin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)
IT 1406-16-2, Vitamin D 1406-16-2D, Vitamin D, derivs. 9007-12-9, Calcitonin 12001-79-5, Vitamin K 12001-79-5D, Vitamin K, derivs. 67763-96-6, IGF I 67763-97-7, IGF II 193830-08-9, Protein GDF5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)
IT 7440-70-2D, Calcium, salts
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dietary, codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)
IT 55396-63-9P, [2-(Pyridin-2-yl)-3H-benzimidazol-5-yl]amine 689295-77-0P,

[2-(Oxazol-4-yl)-3H-benzimidazol-5-yl]amine 689295-78-1P, [2-(1H-Pyrazol-3-yl)-3H-benzimidazol-5-yl]amine 689295-79-2P, [2-(1-Methyl-1H-pyrazol-3-yl)-3H-benzimidazol-5-yl]amine
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate and for effecting bone turnover marker; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT 689295-80-5P, 1-[2-(3-Fluorophenyl)ethyl]-3-[2-(thiazol-4-yl)-3H-benzimidazol-5-yl]urea 689295-81-6P, 6-[[[(3,5-Difluorophenyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689295-82-7P, 6-[[[(3,5-Difluorophenyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689295-83-8P, 1-Phenyl-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]cyclopropanecarboxamide 689295-84-9P, (2S)-2-Hydroxy-2-phenyl-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]propanamide 689295-85-0P, 2-(4-Chloro-3-nitrophenyl)-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]acetamide 689295-87-2P, 6-[[[(3-Nitrophenyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-1H-benzimidazole trifluoroacetate 689295-88-3P, 1-Isopropyl-1-phenyl-3-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]urea 689295-89-4P, 1-((1R)-1-Phenylpropyl)-3-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]urea 689295-90-7P, 1-(3,5-Dichlorobenzyl)-3-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]urea 689295-91-8P, 1-Benzyl-3-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]urea 689295-92-9P, 1-Butyl-3-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]urea 689295-93-0P, 1-(2-Phenylethyl)-3-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]urea 689295-94-1P, 1-(2-Methylbenzyl)-3-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]urea 689295-95-2P, 1-(2-Fluorobenzyl)-3-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]urea 689295-96-3P, 1-(2-Chlorobenzyl)-3-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]urea 689295-97-4P, 1-((1S)-1-Phenylethyl)-3-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]urea 689295-98-5P, 1-(3-Fluorobenzyl)-3-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]urea 689295-99-6P, 1-(4-Methylbenzyl)-3-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]urea 689296-00-2P, 1-(4-Fluorobenzyl)-3-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]urea 689296-01-3P, 1-(2,4-Dichlorobenzyl)-3-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]urea 689296-02-4P, 1-(3,4-Dichlorobenzyl)-3-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]urea 689296-03-5P, 1-(4-Methoxyphenyl)-3-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]urea 689296-04-6P, 1-(3-Methylbenzyl)-3-[2-(thiazol-4-yl)-1H-benzimidazol-6-yl]urea 689296-05-7P, 1-(2-Phenylcyclopropyl)-3-[2-(thiazol-4-yl)-1H-benzimidazol-6-yl]urea 689296-06-8P, 1-(4-Bromobenzyl)-3-[2-(thiazol-4-yl)-1H-benzimidazol-6-yl]urea 689296-07-9P, 1-(4-Methoxybenzyl)-3-[2-(thiazol-4-yl)-1H-benzimidazol-6-yl]urea 689296-08-0P, 6-[[[(3-Methylphenyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-1H-benzimidazole 689296-09-1P, 6-[[[((1R)-1-Phenylethyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-10-4P, 6-[[[[1-(1-Naphthyl)ethyl]amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-11-5P, 1-Methyl-1-phenyl-3-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]urea 689296-12-6P, 1-Benzyl-1-methyl-3-[2-(thiazol-4-yl)-1H-benzimidazol-6-yl]urea 689296-13-7P, N-[2-(Thiazol-4-yl)-1H-benzimidazol-6-yl]-3,4-dihydroisoquinoline-2(1H)-carboxamide 689296-14-8P, N-[2-(Thiazol-4-yl)-1H-benzimidazol-6-yl]-3,4-dihydroquinoline-1(2H)-carboxamide 689296-15-9P, 1-Ethyl-1-phenyl-3-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]urea 689296-16-0P, 6-[[[Methyl(2-methylphenyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-17-1P, 6-[[[Methyl(3-methylphenyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-18-2P, 6-[[[Methyl(4-methylphenyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-19-3P, 1-(4-Hydroxyphenyl)-1-methyl-3-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]urea 689296-20-6P, 6-[[[(sec-Butyl)(phenyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-21-7P, 6-[[[Allyl(phenyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-22-8P, 6-[[[(2-Hydroxyethyl)(phenyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-23-9P, 1-(2-Chlorophenyl)-1-methyl-3-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]urea 689296-24-0P, 6-[[[(3-Chlorophenyl)(methyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-25-1P, 6-[[[(4-Chlorophenyl)(methyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-26-2P, 6-[[[(2-Cyanoethyl)(phenyl)amino]carbonyl]am

ino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-27-3P, 6-[[[Methyl[4-(trifluoromethoxy)phenyl]amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-28-4P, 6-[[[(3,4-Dichlorophenyl)(methyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-29-5P, 6-[[[(2,4-Difluorophenyl)(methyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-30-8P, 6-[[[Benzyl(phenyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-31-9P, 6-[[[Methyl(1-naphthyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-32-0P, 6-[[[(Phenyl)(1-phenylethyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-33-1P, 6-[[[Cyclohexyl(phenyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-34-2P, 1-(1-Phenylcyclopropyl)-3-[2-(thiazol-4-yl)-1H-benzimidazol-6-yl]urea 689296-35-3P, 6-[[[(1-Methyl-1-phenylethyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-36-4P, 6-[[[((1S)-1-Phenylpropyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-37-5P, 6-[[[(3-Chlorobenzyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-38-6P, 6-[[[(2,5-Dichlorobenzyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-39-7P, 2-(Thiazol-4-yl)-6-[[[[3-(trifluoromethyl)benzyl]amino]carbonyl]amino]-3H-benzimidazole 689296-40-0P, 6-[[[Benzyl(ethyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-41-1P, 6-[[[Methyl((1R)-1-phenylethyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-42-2P, 6-[[[Methyl((1S)-1-phenylethyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-43-3P, 6-[[(2-Phenylpyrrolidin-1-yl)carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-44-4P, 6-[[[(4-Methoxyphenyl)(methyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-45-5P, 6-[[[(3,5-Dimethylphenyl)(methyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-46-6P, 6-[[[(5-Isopropyl-2-methylphenyl)(methyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-47-7P, 6-[[[(6-Methoxypyridin-2-yl)(methyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-48-8P, 6-[[[Ethyl(3-methylbenzyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-49-9P, 6-[[[(3,4-Dichlorobenzyl)(methyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-50-2P, 6-[[[[(2-Bromothien-3-yl)methyl]amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-51-3P, 6-[[[Methyl[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-52-4P, 6-[[[(2,4-Dichlorophenyl)(methyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-53-5P, 1-Cyclopropyl-1-phenyl-3-[2-(thiazol-4-yl)-1H-benzimidazol-6-yl]urea 689296-54-6P, 1-[4-(Hydroxymethyl)phenyl]-1-methyl-3-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]urea 689296-55-7P, 1-Methyl-3-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]-1-[2-(trifluoromethoxy)phenyl]urea 689296-56-8P, 3-Phenyl-N-[2-(thiazol-4-yl)-3H-benzimidazol-5-yl]propionamide 689296-57-9P, 2-Phenoxy-N-[2-(thiazol-4-yl)-3H-benzimidazol-5-yl]acetamide 689296-58-0P, trans-5-[[1-(2-Phenylcyclopropyl)methanoyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-59-1P, 5-(4-Phenylbutanoylamino)-2-(thiazol-4-yl)-3H-benzimidazole 689296-60-4P, 6-(3-Phenylbutanoylamino)-2-(thiazol-4-yl)-1H-benzimidazole 689296-61-5P, (1R,2R)-2-Phenylcyclopropanecarboxylic acid N-[2-(thiazol-4-yl)-3H-benzimidazol-5-yl]amide 689296-63-7P, (1S,2S)-2-Phenylcyclopropanecarboxylic acid N-[2-(thiazol-4-yl)-3H-benzimidazol-5-yl]amide 689296-65-9P, 2-Methyl-3-phenyl-N-[2-(thiazol-4-yl)-3H-benzimidazol-5-yl]propionamide 689296-67-1P, 5-(2-Phenylbutanoylamino)-2-(thiazol-4-yl)-3H-benzimidazole 689296-70-6P, 5-(2,3-Diphenylpropanoylamino)-2-(thiazol-4-yl)-3H-benzimidazole 689296-72-8P, 5-(2,2-Diphenylethanoylamino)-2-(thiazol-4-yl)-3H-benzimidazole 689296-73-9P, 5-(3-Cyclohexylpropanoylamino)-2-(thiazol-4-yl)-3H-benzimidazole 689296-75-1P, 5-[[2-(Bicyclo[2.2.1]hept-2-yl)ethanoyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689296-77-3P, 6-[(2-Methyl-2-phenylpropanoyl)amino]-2-(thiazol-4-yl)-1H-benzimidazole 689296-79-5P, 6-(2-Phenylpropanoylamino)-2-(thiazol-4-yl)-1H-benzimidazole 689296-81-9P, 6-(2-Methoxy-2-phenylethanoylamino)-2-(thiazol-4-yl)-1H-benzimidazole 689296-83-1P, 6-(2-Hydroxy-2-phenylethanoylamino)-2-(thiazol-4-yl)-1H-benzimidazole 689296-85-3P, 6-(2-Hydroxy-2-phenylpropanoylamino)-2-(thiazol-4-yl)-1H-benzimidazole 689296-86-4P, 6-[[2-(Indan-2-yl)ethanoyl]amino]-2-(thiazol-4-yl)-1H-benzimidazole 689296-88-6P, 6-[[1-(Indan-1-yl)methanoyl]amino]-2-(thiazol-4-yl)-1H-

benzimidazole 689296-90-0P, 6-[(2-Cyclopentyl-2-phenylethanoyl)amino]-2-(thiazol-4-yl)-1H-benzimidazole 689296-93-3P, 6-[(2-Cyclohexyl-2-phenylethanoyl)amino]-2-(thiazol-4-yl)-1H-benzimidazole 689296-96-6P, 6-[[2-(3,4-Dichlorophenyl)ethanoyl]amino]-2-(thiazol-4-yl)-1H-benzimidazole 689296-99-9P, 6-[[1-(1-Phenylcyclopentyl)methanoyl]amino]-2-(thiazol-4-yl)-1H-benzimidazole 689297-02-7P, 6-(3,3-Diphenylpropanoylamino)-2-(thiazol-4-yl)-1H-benzimidazole 689297-05-0P, 6-[[2-(Biphenyl-4-yl)ethanoyl]amino]-2-(thiazol-4-yl)-1H-benzimidazole 689297-08-3P, (3S)-3-Phenyl-N-[2-(thiazol-4-yl)-3H-benzimidazol-5-yl]butyramide 689297-11-8P, (3R)-3-Phenyl-N-[2-(thiazol-4-yl)-3H-benzimidazol-5-yl]butyramide 689297-14-1P, (2R)-2-Phenyl-N-[2-(thiazol-4-yl)-3H-benzimidazol-5-yl]butyramide 689297-16-3P, 6-[[2-(3-Fluorophenyl)ethanoyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689297-18-5P, 2-(3-Chlorophenyl)-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]acetamide 689297-20-9P, 6-[[2-(3-Methoxyphenyl)ethanoyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689297-22-1P, N-[2-(Thiazol-4-yl)-1H-benzimidazol-5-yl]-2-(4-trifluoromethylphenyl)acetamide 689297-24-3P, N-[2-(Thiazol-4-yl)-1H-benzimidazol-5-yl]-2-(p-tolyl)acetamide 689297-26-5P, 6-[[2-(4-Nitrophenyl)ethanoyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689297-28-7P, N-[2-(Thiazol-4-yl)-1H-benzimidazol-5-yl]-2-(3-trifluoromethylphenyl)acetamide 689297-30-1P, 6-[[2-(3-Nitrophenyl)ethanoyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689297-32-3P, 6-[[2-(4-Fluorophenyl)ethanoyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689297-34-5P, 6-[[2-[3,5-Bis(trifluoromethyl)phenyl]ethanoyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689297-36-7P, 2-(4-Chlorophenyl)-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]acetamide 689297-38-9P, 2-(3,4-Difluorophenyl)-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]acetamide 689297-40-3P, 6-[[2-(4-Methoxyphenyl)ethanoyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689297-42-5P, 2-(3,5-Dimethylphenyl)-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]acetamide 689297-44-7P, 2-(3,5-Difluorophenyl)-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]acetamide 689297-46-9P, 6-[[2-(4-Isopropylphenyl)ethanoyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689297-48-1P, 6-[[2-(3-Fluoro-4-methoxyphenyl)ethanoyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689297-50-5P, N-[2-(Thiazol-4-yl)-1H-benzimidazol-5-yl]-2-(3,4,5-trifluorophenyl)acetamide 689297-52-7P, 2-(4-Nitrophenyl)-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]propionamide 689297-54-9P, 6-[[2-(4-Hydroxyphenyl)propanoyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689297-56-1P, 2-(4-Chlorophenyl)-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]propionamide 689297-58-3P, 6-[[2-(Benzodioxol-5-yl)ethanoyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole 689297-59-4P, 2-(4-Chlorophenyl)-2-hydroxy-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]acetamide 689297-60-7P, 3-Methyl-2-phenyl-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]butyramide 689297-61-8P, (2R)-2-(4-Chlorophenyl)-2-hydroxy-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]ethanamide 689297-62-9P, (2S)-2-(4-Chlorophenyl)-2-hydroxy-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]ethanamide 689297-64-1P, (2R)-3-Methyl-2-phenyl-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]butyramide 689297-66-3P, (2S)-3-Methyl-2-phenyl-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]butyramide 689297-68-5P, 3-(3-Chlorophenyl)-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]butyramide 689297-70-9P, (2R)-2-Hydroxy-2-phenyl-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]propionamide 689297-72-1P, 2-(4-Chlorophenyl)-3-methyl-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]butyramide 689297-74-3P, (2R)-2-(4-Chlorophenyl)-3-methyl-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]butyramide 689297-75-4P, (2S)-2-(4-Chlorophenyl)-3-methyl-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]butyramide 689297-77-6P, 3-(4-Methylphenyl)-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]butanamide 689297-78-7P, 3-(3-Fluorophenyl)-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]butanamide 689297-79-8P, 3-(4-Fluorophenyl)-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]butanamide 689297-80-1P, 3-(4-Chlorophenyl)-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]butanamide 689297-81-2P, 3-(2-Fluorophenyl)-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]butanamide 689297-83-4P, 2-(4-Fluorophenyl)-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]propanamide 689297-84-5P, 1-(4-Chlorophenyl)-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]cyclopropanecarboxamide 689297-85-6P, 1-(3-Fluorophenyl)-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]cyclopropanecarboxamide 689297-87-8P, 1-(3-Chlorophenyl)-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]cyclopropanecarboxamide 689297-89-0P, 1-(3,5-Dichlorophenyl)-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]cyclopropanecarboxamide

689297-91-4P, 1-(3,5-Difluorophenyl)-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]cyclopropanecarboxamide 689297-93-6P, 2-Hydroxy-3-methyl-2-phenyl-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]butanamide 689297-95-8P, (2R)-2-Hydroxy-3-methyl-2-phenyl-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]butanamide 689297-97-0P, (2S)-2-Hydroxy-3-methyl-2-phenyl-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]butanamide 689297-99-2P, 2-Cyclopropyl-2-hydroxy-2-phenyl-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]acetamide 689298-01-9P, 2-(3-Chlorophenyl)-2-hydroxy-3-methyl-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]butanamide 689298-03-1P, (2R)-2-(3-Chlorophenyl)-2-hydroxy-3-methyl-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]butanamide 689298-04-2P, (2S)-2-(3-Chlorophenyl)-2-hydroxy-3-methyl-N-[2-(thiazol-4-yl)-1H-benzimidazol-5-yl]butanamide 689298-07-5P 689298-08-6P, 6-[[[(3-Methylphenyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-1H-benzimidazole trifluoroacetate 689298-09-7P, 6-[[[((1R)-1-Phenylethyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-10-0P, 6-[[[[1-(1-Naphthyl)ethyl]amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-11-1P, 6-[[[Methyl(2-methylphenyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-13-3P, 6-[[[Methyl(3-methylphenyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-14-4P, 6-[[[Methyl(4-methylphenyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-15-5P, 6-[[[(sec-Butyl)(phenyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-16-6P, 6-[[[Allyl(phenyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-17-7P, 6-[[[(2-Hydroxyethyl)(phenyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-18-8P, 6-[[[(4-Hydroxyphenyl)(methyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-19-9P, 6-[[[(3-Chlorophenyl)(methyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-20-2P, 6-[[[(4-Chlorophenyl)(methyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-22-4P, 6-[[[(2-Cyanoethyl)(phenyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-23-5P, 6-[[[Methyl[4-(trifluoromethoxy)phenyl]amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-24-6P, 6-[[[(3,4-Dichlorophenyl)(methyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-25-7P, 6-[[[(2,4-Difluorophenyl)(methyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-26-8P, 6-[[[Benzyl(phenyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-27-9P, 6-[[[Methyl(1-naphthyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-28-0P, 6-[[[(Phenyl)(1-phenylethyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-29-1P, 6-[[[Cyclohexyl(phenyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-30-4P, 6-[[[(1-Methyl-1-phenylethyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-31-5P, 6-[[[((1R)-1-Phenylpropyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-32-6P, 6-[[[((1S)-1-Phenylpropyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-34-8P, 6-[[[(3-Chlorobenzyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-36-0P, 6-[[[(2,5-Dichlorobenzyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-38-2P, 6-[[[(3,5-Dichlorobenzyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-40-6P, 2-(Thiazol-4-yl)-6-[[[[3-(trifluoromethyl)benzyl]amino]carbonyl]amino]-3H-benzimidazole trifluoroacetate 689298-42-8P, 6-[[[Benzyl(ethyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-44-0P, 6-[[[Methyl((1R)-1-phenylethyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-46-2P, 6-[[[Methyl((1S)-1-phenylethyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-48-4P, 6-[[(2-Phenylpyrrolidin-1-yl)carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-50-8P

, 6-[[[(2-Phenylcyclopropyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-52-0P, 6-[[[(4-Methoxyphenyl)(methyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-53-1P, 6-[[[(3,5-Dimethylphenyl)(methyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-54-2P, 6-[[[(5-Isopropyl-2-methylphenyl)(methyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-55-3P, 6-[[[(6-Methoxypyridin-2-yl)(methyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole bis(trifluoroacetate) 689298-56-4P, 6-[[[Ethyl(3-methylbenzyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-57-5P, 6-[[[(3,4-Dichlorobenzyl)(methyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-58-6P, 6-[[[[(2-Bromothien-3-yl)methyl]amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-59-7P, 6-[[[Methyl[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole bis(trifluoroacetate) 689298-60-0P, 6-[[[(2,4-Dichlorophenyl)(methyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-61-1P, 6-[[[Isopropyl(phenyl)amino]carbonyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-63-3P, trans-5-[[1-(2-Phenylcyclopropyl)methanoyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-65-5P, 5-(4-Phenylbutanoylamino)-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-66-6P, 6-(3-Phenylbutanoylamino)-2-(thiazol-4-yl)-1H-benzimidazole trifluoroacetate 689298-68-8P, 5-[[1-(1-Phenylcyclopropyl)methanoyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-70-2P, 5-(2,3-Diphenylpropanoylamino)-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-72-4P, 5-(2,2-Diphenylethanoylamino)-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-74-6P, 5-(3-Cyclohexylpropanoylamino)-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-76-8P, 5-[[2-(Bicyclo[2.2.1]hept-2-yl)ethanoyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-77-9P, 6-[(2-Methyl-2-phenylpropanoyl)amino]-2-(thiazol-4-yl)-1H-benzimidazole trifluoroacetate 689298-78-0P, 6-(2-Phenylpropanoylamino)-2-(thiazol-4-yl)-1H-benzimidazole trifluoroacetate 689298-79-1P, 6-(2-Methoxy-2-phenylethanoylamino)-2-(thiazol-4-yl)-1H-benzimidazole trifluoroacetate 689298-80-4P, 6-(2-Hydroxy-2-phenylethanoylamino)-2-(thiazol-4-yl)-1H-benzimidazole trifluoroacetate 689298-81-5P, 6-(2-Hydroxy-2-phenylpropanoylamino)-2-(thiazol-4-yl)-1H-benzimidazole trifluoroacetate 689298-82-6P, 6-[[2-(Indan-2-yl)ethanoyl]amino]-2-(thiazol-4-yl)-1H-benzimidazole trifluoroacetate 689298-83-7P, 6-[[1-(Indan-1-yl)methanoyl]amino]-2-(thiazol-4-yl)-1H-benzimidazole trifluoroacetate 689298-84-8P, 6-[(2-Cyclopentyl-2-phenylethanoyl)amino]-2-(thiazol-4-yl)-1H-benzimidazole trifluoroacetate 689298-85-9P, 6-[(2-Cyclohexyl-2-phenylethanoyl)amino]-2-(thiazol-4-yl)-1H-benzimidazole trifluoroacetate 689298-86-0P, 6-[[2-(3,4-Dichlorophenyl)ethanoyl]amino]-2-(thiazol-4-yl)-1H-benzimidazole trifluoroacetate 689298-87-1P, 6-[[1-(1-Phenylcyclopentyl)methanoyl]amino]-2-(thiazol-4-yl)-1H-benzimidazole trifluoroacetate 689298-88-2P, 6-(3,3-Diphenylpropanoylamino)-2-(thiazol-4-yl)-1H-benzimidazole trifluoroacetate 689298-89-3P, 6-[[2-(Biphenyl-4-yl)ethanoyl]amino]-2-(thiazol-4-yl)-1H-benzimidazole trifluoroacetate 689298-90-6P, 6-[[2-(3-Fluorophenyl)ethanoyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-91-7P, 6-[[2-(3-Methoxyphenyl)ethanoyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-92-8P, 6-[[2-(4-Nitrophenyl)ethanoyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-93-9P, 6-[[2-(3-Nitrophenyl)ethanoyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-94-0P, 6-[[2-(4-Fluorophenyl)ethanoyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-95-1P, 6-[[2-[3,5-Bis(trifluoromethyl)phenyl]ethanoyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-96-2P, 6-[[2-(4-Methoxyphenyl)ethanoyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-97-3P, 6-[[2-(4-Isopropylphenyl)ethanoyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-98-4P, 6-[[2-(3-Fluoro-4-methoxyphenyl)ethanoyl]amino]-2-(thiazol-4-yl)-3H-benzimidazole trifluoroacetate 689298-99-5P, 6-[[2-(4-Hydroxyphenyl)propanoyl]amino]-2-

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RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate and for effecting bone turnover marker; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT 9028-35-7, HMG-CoA reductase 94716-09-3, Cathepsin K 165245-96-5, p38 Kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT 47931-85-1, Salmon calcitonin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nasal spray, codrug; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT 404-70-6, 3-Fluorophenethylamine 3973-08-8, Thiazole-4-carboxylic acid 5307-14-2, 2-Nitrobenzene-1,4-diamine 6120-95-2, 1-Phenylcyclopropane-1-carboxylic acid 13113-71-8, (2S)-2-Hydroxy-2-phenylpropionic acid 83594-83-6, 3,5-Difluorophenyl isocyanate
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT 25893-06-5P, [2-(Thiazol-4-yl)-3H-benzimidazol-5-yl]amine 219492-81-6P, (4-Amino-3-nitrophenyl)carbamic acid tert-butyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT 9000-83-3, Vacuolar ATPase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(proton-translocating, vacuolar, osteoclast, inhibitors, codrugs; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

IT 83462-55-9, Deoxypyridinoline
RL: ANT (Analyte); ANST (Analytical study)
(urinary, method of effecting bone turnover marker using; preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators)

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ACCESSION NUMBER: 2004:412750 CAPLUS
DOCUMENT NUMBER: 140:423687
TITLE: Preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors
INVENTOR(S): Hartman, George D.; Hoffman, Jacob M.; Smith, Anthony M.; Tucker, Thomas J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004041164 | A2 | 20040521 | WO 2003-US34100 | 20031024 |
| WO 2004041164 | A3 | 20041007 | | |

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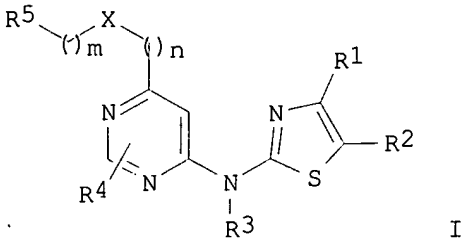
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2503715 AA 20040521 CA 2003-2503715 20031024
EP 1558609 A2 20050803 EP 2003-779322 20031024
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
PRIORITY APPLN. INFO.: US 2002-422313P P 20021030
WO 2003-US34100 W 20031024
OTHER SOURCE(S): MARPAT 140:423687
GI



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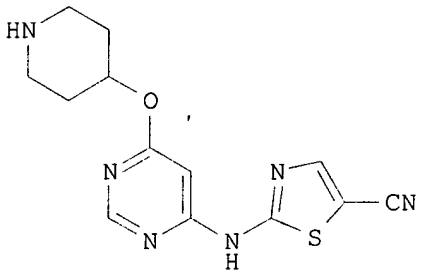

II

AB Title compds. I [X = O, S, amino; m,n = 0-3; R1-2, R4 = H, OH, alkoxy, CN, etc.; R3 = H, sulfonyl, acyl, carboxy, etc.; R5 = heterocyclyl] are prepared For instance, tert-Bu 4-[(6-aminopyrimidin-4-yl)oxy]piperidine-1-carboxylate (preparation given) is reacted with 2-chlorothiazole-5-carbonitrile (THF, NaH) and the resulting product deprotected (CH2Cl2, TFA) to give II. I inhibit, regulate and/or modulate kinase signal transduction; they are useful in the treatment of kinase-dependent diseases and conditions, such as angiogenesis, cancer, tumor growth, atherosclerosis, age related macular degeneration, retinal ischemia, macular edema, diabetic retinopathy and inflammatory diseases.

IT Troponins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(I, combination pharmaceutical; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Lung, neoplasm
(adenocarcinoma; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Meningitis
(bacterial, tissue damage from, treatment; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Mammary gland, neoplasm
(carcinoma; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Intestine, neoplasm
(colorectal; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Antihypertensives
Antitumor agents
Cytotoxic agents
(combination pharmaceutical; preparation of thiazolylamino-substituted

pyrimidines as kinase inhibitors)
IT Gonadotropins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)
IT Photodynamic therapy
(combination therapy; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)
IT Dermatitis
(contact; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)
IT Allergy
(delayed hypersensitivity; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)
IT Eye, disease
(diabetic retinopathy; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)
IT Uterus, disease
(endometriosis; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)
IT Growth factors, animal
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fibroblast-derived growth factors, inhibitor, combination pharmaceutical; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)
IT Neuroglia, neoplasm
(glioblastoma; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)
IT Lymphoma
(histiocytic; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)
IT Ovary, disease
(hyperstimulation syndrome; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)
IT Integrins
Interleukin 12
Platelet-derived growth factors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor, combination pharmaceutical; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)
IT Eye, disease
(macula, senile degeneration; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)
IT Carcinoma
(mammary; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)
IT Androgen receptors
Estrogen receptors
Retinoid receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(modulator, combination pharmaceutical; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)
IT Angiogenesis inhibitors
Anti-inflammatory agents
Antiarthritics
Bone, disease
Eye, disease
Human
Larynx, neoplasm
Leukemia
Lung, neoplasm
Neoplasm
Pancreas, neoplasm
Preeclampsia
Psoriasis
Rickets

Stomach, neoplasm
(preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Carcinoma
(pulmonary adenocarcinoma; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Carcinoma
(pulmonary small-cell; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Lung, neoplasm
(small-cell carcinoma; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Interferons
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α, inhibitor, combination pharmaceutical; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Integrins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(αIIbβ3, antagonist, combination pharmaceutical; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(γ, agonist, combination pharmaceutical; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT 127464-60-2, Vascular endothelial growth factor
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibody to, combination pharmaceutical; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT 50-35-1, Thalidomide 911-45-5, **Clomifene** 9002-67-9, Luteinizing hormone 9002-68-0, Follicle stimulating hormone 10540-29-1, Tamoxifen 25614-03-3, Bromocriptine 33069-62-4, Paclitaxel 37300-21-3, Pentosan polysulfate 84449-90-1, Raloxifene 86090-08-6, Angiostatin 99519-84-3, Carboxyamidotriazole 110942-08-0, Luprolide 117048-59-6, Combretastatin A-4 144494-65-5, Tirofiban 148717-90-2, Squalamine 180288-69-1, Trastuzumab 561321-04-8, 6-(O-Chloroacetylcarbonyl)fumagillol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT 9028-35-7, HMG-CoA reductase 9068-38-6, Reverse transcriptase 39391-18-9, Cyclooxygenase 131384-38-8, Prenylprotein transferase 141907-41-7, Matrix metalloproteinase 144114-21-6, **HIV** protease 329900-75-6, COX-2
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor, combination pharmaceutical; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT 150428-23-2, Cyclin-dependent kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT 436852-23-2P, 2-[(6-Chloro-2-methylpyrimidin-4-yl)amino]-1,3-thiazole-5-carbonitrile 691400-75-6P, tert-Butyl 4-[[6-[(5-cyano-1,3-thiazol-2-yl)amino]pyrimidin-4-yl]oxy]piperidine-1-carboxylate 691400-79-0P, tert-Butyl 4-[[6-[(5-phenyl-1,3-thiazol-2-yl)amino]pyrimidin-4-yl]oxy]piperidine-1-carboxylate 691400-82-5P 691400-85-8P, tert-Butyl 4-[[[6-[(5-phenyl-1,3-thiazol-2-yl)amino]pyrimidin-4-yl]oxy]methyl]piperidine-1-carboxylate 691400-91-6P, 2-[[2-Methyl-6-(piperidin-4-yloxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691400-99-4P, 2-[[2-Methyl-6-(piperidin-4-ylmethoxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691401-00-0P 691401-17-9P, tert-Butyl [4-[[[6-[(5-cyano-1,3-thiazol-2-yl)amino]-2-methylpyrimidin-4-yl]oxy]methyl]piperidin-1-yl]acetate 691401-18-0P, [4-[[[6-[(5-Cyano-1,3-thiazol-2-yl)amino]-2-methylpyrimidin-4-yl]oxy]methyl]piperidin-1-yl]acetic acid 691401-45-3P, tert-Butyl 4-[[6-[(5-cyanothiazol-2-yl)amino]-2-methylpyrimidin-4-yl]amino]piperidine-1-carboxylate

691401-48-6P, tert-Butyl 4-[[6-[[(5-cyano-1,3-thiazol-2-yl)amino]methyl]-2-methylpyrimidin-4-yl]amino]piperidine-1-carboxylate
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT 691400-77-8P, 2-[[6-(Piperidin-4-yloxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691400-78-9P, 2-[[6-(Piperidin-4-yloxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691400-80-3P, N-(5-Phenyl-1,3-thiazol-2-yl)-6-(piperidin-4-yloxy)pyrimidin-4-amine 691400-81-4P, N-(5-Phenyl-1,3-thiazol-2-yl)-6-(piperidin-4-yloxy)pyrimidin-4-amine trifluoroacetate 691400-83-6P, 2-[[6-(Piperidin-4-ylmethoxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691400-84-7P, 2-[[6-(Piperidin-4-ylmethoxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691400-86-9P, N-(5-Phenyl-1,3-thiazol-2-yl)-6-(piperidin-4-ylmethoxy)pyrimidin-4-amine 691400-87-0P, N-(5-Phenyl-1,3-thiazol-2-yl)-6-(piperidin-4-ylmethoxy)pyrimidin-4-amine trifluoroacetate 691400-90-5P, 2-[[2-Methyl-6-(piperidin-4-yloxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691400-92-7P, N-(5-Phenyl-1,3-thiazol-2-yl)-6-(piperidin-4-yloxy)-2-methylpyrimidin-4-amine 691400-93-8P 691400-94-9P, 2-[[2-Methyl-6-((3R)-pyrrolidin-3-yloxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691400-95-0P, 2-[[2-Methyl-6-((3R)-pyrrolidin-3-yloxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691400-96-1P, 2-[[2-Methyl-6-((3S)-pyrrolidin-3-yloxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691400-97-2P, 2-[[2-Methyl-6-((3S)-pyrrolidin-3-yloxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691400-98-3P, 2-[[2-Methyl-6-(piperidin-4-ylmethoxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-01-1P, 2-[[2-Methyl-6-(morpholin-2-ylmethoxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-02-2P, 2-[[2-Methyl-6-(morpholin-2-ylmethoxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691401-03-3P, 2-[[2-Methyl-6-(tetrahydro-2-pyran-4-yloxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-04-4P, 2-[[2-Methyl-6-(tetrahydro-2-pyran-4-yloxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691401-05-5P, 2-[[2-Isopropyl-6-(piperidin-4-yloxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-06-6P, 2-[[2-Isopropyl-6-(piperidin-4-yloxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691401-11-3P, 2-[[2-Methyl-6-[[1-(2-(morpholin-4-yl)ethyl)piperidin-4-yl]oxy]pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-15-7P, 2-[4-[[6-[(5-Cyano-1,3-thiazol-2-yl)amino]-2-methylpyrimidin-4-yl]oxy]piperidin-1-yl]-N-isopropylacetamide 691401-16-8P 691401-19-1P, N-(tert-Butyl)-2-[4-[[[6-[(5-cyano-1,3-thiazol-2-yl)amino]-2-methylpyrimidin-4-yl]oxy]methyl]piperidin-1-yl]acetamide 691401-20-4P, 2-[[2-Methyl-6-(3-(morpholin-4-yl)propoxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-21-5P, 2-[[2-Methyl-6-(3-(morpholin-4-yl)propoxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691401-22-6P, 2-[[2-Methyl-6-(2-(morpholin-4-yl)ethoxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-23-7P, 2-[[2-Methyl-6-(2-(morpholin-4-yl)ethoxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691401-24-8P, 2-[[2-Methyl-6-(2-(piperidin-1-yl)ethoxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-25-9P 691401-26-0P, 2-[[2-Methyl-6-[(2-(morpholin-4-yl)ethyl)amino]pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-27-1P, 2-[[2-Methyl-6-[(2-(morpholin-4-yl)ethyl)amino]pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691401-29-3P, 2-[[6-[(3-(Morpholin-4-yl)propyl)amino]pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-30-6P, 2-[[6-[(3-(Morpholin-4-yl)propyl)amino]pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691401-31-7P, 2-[[2-Methyl-6-(tetrahydro-2H-pyran-4-ylamino)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-32-8P, 2-[[6-[[3-(1H-Imidazol-1-yl)propyl]amino]-2-methylpyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-33-9P 691401-34-0P 691401-35-1P, 2-[[6-[(1,4-Dioxan-2-ylmethyl)amino]-2-methylpyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-36-2P, 2-[[6-[((1,4-Dioxan-2-yl)methyl)amino]-2-methylpyrimidin-4-yl]amino]thiazole-5-carbonitrile trifluoroacetate 691401-37-3P 691401-38-4P 691401-40-8P, 2-[[2-Methyl-6-(tetrahydrofuran-3-

ylamino)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-41-9P, 2-[[2-Methyl-6-(tetrahydrofuran-3-ylamino)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691401-44-2P, 2-[4-[[6-[(5-Cyanothiazol-2-yl)amino]-2-methylpyrimidin-4-yl]amino]piperidin-1-yl]-N-isopropylacetamide trifluoroacetate 691401-46-4P, 2-[[2-Methyl-6-(piperidin-4-ylamino)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-47-5P, 2-[[2-Methyl-6-(piperidin-4-ylamino)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691401-49-7P, 2-[[2-Methyl-6-[(piperidin-4-ylmethyl)amino]pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-50-0P, 2-[[2-Methyl-6-[(piperidin-4-ylmethyl)amino]pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691401-52-2P, 2-[[5-Methyl-6-(piperidin-4-ylamino)pyrimidin-4-yl]oxy]-1,3-thiazole-5-carbonitrile 691401-53-3P, 2-[[5-Methyl-6-(piperidin-4-ylamino)pyrimidin-4-yl]oxy]-1,3-thiazole-5-carbonitrile trifluoroacetate 691401-55-5P, 2-[[2-Methyl-6-[(2-(morpholin-4-yl)ethyl)thio]pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-59-9P, 2-[[6-(Piperidin-4-ylthio)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-60-2P, 2-[[6-(Piperidin-4-ylthio)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691401-61-3P, 2-[4-[[6-((5-Cyanothiazol-2-yl)amino)-2-methylpyrimidin-4-yl]amino]piperidin-1-yl]-N-isopropylacetamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT 75-31-0, Isopropylamine, reactions 75-64-9, tert-Butylamine, reactions 123-00-2, 3-(Morpholin-4-yl)propan-1-amine 622-40-2, 2-(Morpholin-4-yl)ethanol 767-16-8, 6-Amino-2-methylpyrimidin-4-ol 1193-22-2, 4-Hydroxy-6-aminopyrimidine 1749-68-4, 6-Chloro-2-methylpyrimidin-4-amine 1850-98-2, 2-Isopropyl-4,6-dichloropyrimidine 2038-03-1, 4-(2-Aminoethyl)morpholine 2081-44-9, Tetrahydro-2H-pyran-4-ol 3040-44-6, 2-Piperidin-1-ylethanol 3647-69-6, 4-(2-Chloroethyl)morpholine hydrochloride 5036-48-6, 3-(1H-Imidazol-1-yl)propan-1-amine 5292-43-3, tert-Butyl bromoacetate 6338-70-1 20120-24-5, Ethyl 3-(morpholin-4-yl)propanoate 38041-19-9, Tetrahydro-2H-pyran-4-amine 45697-13-0 51640-36-9, 2-Chloro-1,3-thiazole-5-carbonitrile 73874-95-0, tert-Butyl piperidin-4-ylcarbamate 75726-96-4, 2-Bromo-N-isopropylacetamide 87120-72-7, tert-Butyl 4-aminopiperidine-1-carboxylate 101469-92-5, tert-Butyl (S)-3-hydroxypyrrolidine-1-carboxylate 109384-19-2, tert-Butyl 4-hydroxypiperidine-1-carboxylate 109431-87-0, tert-Butyl (R)-3-hydroxypyrrolidine-1-carboxylate 123855-51-6, tert-Butyl 4-(hydroxymethyl)piperidine-1-carboxylate 144222-22-0, tert-Butyl 4-aminomethylpiperidine-1-carboxylate 154917-45-0, 1,4-Dioxan-2-ylmethylamine 189321-66-2, 4-(tert-Butoxycarbonyl)morpholine-2-carboxylic acid 204512-94-7, Tetrahydrofuran-3-amine hydrochloride 329794-40-3, 2-Chloro-5-phenyl-1,3-thiazole 436851-99-9, 2-[(6-Chloropyrimidin-4-yl)amino]-1,3-thiazole-5-carbonitrile 436852-24-3, 2-[(6-Chloro-5-methylpyrimidin-4-yl)amino]-1,3-thiazole-5-carbonitrile 691401-39-5, 2-[(6-Methoxy-2-methylpyrimidin-4-yl)amino]-1,3-thiazole-5-carbonitrile 691401-58-8, tert-Butyl 4-[(6-aminopyrimidin-4-yl)thio]piperidine-1-carboxylate
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT 4441-30-9P, 3-(Morpholin-4-yl)propan-1-ol 89280-06-8P, 6-Amino-2-methylpyrimidine-4-thiol 691400-74-5P, tert-Butyl 4-[(6-aminopyrimidin-4-yl)oxy]piperidine-1-carboxylate 691400-88-1P, tert-Butyl 4-[(6-amino-2-methylpyrimidin-4-yl)oxy]piperidine-1-carboxylate 691400-89-2P, tert-Butyl 4-[[6-[(5-cyano-1,3-thiazol-2-yl)amino]-2-methylpyrimidin-4-yl]oxy]piperidine-1-carboxylate 691401-07-7P, 6-Chloro-2-isopropylpyrimidin-4-amine 691401-09-9P 691401-10-2P, 2-Methyl-6-[[1-(2-(morpholin-4-yl)ethyl)piperidin-4-yl]oxy]pyrimidin-4-amine 691401-12-4P, tert-Butyl [4-[[6-[(5-cyano-1,3-thiazol-2-yl)amino]-2-methylpyrimidin-4-yl]oxy]piperidin-1-yl]acetate 691401-14-6P, [4-[[6-[(5-Cyano-1,3-thiazol-2-yl)amino]-2-methylpyrimidin-4-yl]oxy]piperidin-1-yl]acetic acid trifluoroacetate 691401-42-0P, tert-Butyl [1-[2-(isopropylamino)-2-oxoethyl]piperidin-4-yl]carbamate 691401-51-1P 691401-54-4P, 2-Methyl-6-[(2-(morpholin-4-yl)ethyl)thio]pyrimidin-4-amine 691401-56-6P, tert-Butyl

4-[(6-amino-2-methylpyrimidin-4-yl)thio]piperidine-1-carboxylate 691401-57-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT 80449-02-1, Tyrosine kinase
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(related disease, prevention/treatment; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

L23 ANSWER 19 OF 160 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:722925 CAPLUS
DOCUMENT NUMBER: 141:218967
TITLE: Methods and compositions with **trans-clomiphene** for treating wasting and lipodystrophy
INVENTOR(S): Podolski, Joseph S.; Wiehle, Ronald
PATENT ASSIGNEE(S): Zonagen, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 12 pp., Cont.-in-part of U.S. Ser. No. 427,768.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2004171697 | A1 | 20040902 | US 2003-712546 | 20031112 |
| WO 2003005954 | A2 | 20030123 | WO 2002-US21524 | 20020709 |
| WO 2003005954 | A3 | 20031023 | | |
| WO 2003005954 | B1 | 20031204 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2004097597 | A1 | 20040520 | US 2003-427768 | 20030430 |

| PRIORITY APPLN. INFO.: | | |
|---|---|---|
| US 2001-304313P | P | 20010709 |
| WO 2002-US21524 | A2 | 20020709 |
| US 2003-427768 | A2 | 20030430 |

AB The invention discloses compns. and methods useful for treating wasting, especially a loss of muscle mass. The present invention also discloses compns. and methods useful for treating lipodystrophy. The compns. and methods of the present invention are particularly beneficial to **HIV**-infected individuals.

IT Immunostimulants
(adjuvants; methods and compns. with **trans-clomiphene** for treating wasting and lipodystrophy)

IT Drug delivery systems
(carriers; methods and compns. with **trans-clomiphene** for treating wasting and lipodystrophy)

IT **AIDS** (disease)
Blood serum
Body weight
Bone
CD4-positive T cell
Combination chemotherapy
Erythrocyte
Human
Human immunodeficiency virus
Kidney
Lipodystrophy

Liver
Lymphocyte
Osteoblast
Platelet (blood)
(methods and compns. with **trans-clomiphene** for treating wasting and lipodystrophy)

IT Hemoglobins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(methods and compns. with **trans-clomiphene** for treating wasting and lipodystrophy)

IT Antiestrogens
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. with **trans-clomiphene** for treating wasting and lipodystrophy)

IT Muscle
(modulating mass of; methods and compns. with **trans-clomiphene** for treating wasting and lipodystrophy)

IT Disease, animal
(wasting; methods and compns. with **trans-clomiphene** for treating wasting and lipodystrophy)

IT 50-99-7, D-Glucose, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(blood; methods and compns. with **trans-clomiphene** for treating wasting and lipodystrophy)

IT 57-88-5, Cholesterol, biological studies 58-22-0, Testosterone 60-27-5, Creatinine 7440-23-5, Sodium, biological studies 9000-86-6, ALT 9001-78-9, Alkaline phosphatase 9002-62-4, Prolactin, biological studies 9002-67-9, LH 9002-68-0, FSH
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(methods and compns. with **trans-clomiphene** for treating wasting and lipodystrophy)

IT 50-41-9, **Clomid** 15690-55-8, cis-**Clomiphene** 15690-57-0, **trans-Clomiphene**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. with **trans-clomiphene** for treating wasting and lipodystrophy)

L23 ANSWER 20 OF 160 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:214874 CAPLUS
DOCUMENT NUMBER: 143:1418
TITLE: A novel protocol of ovulation induction with delayed gonadotropin-releasing hormone antagonist administration combined with high-dose recombinant follicle-stimulating hormone and **clomiphene** citrate for poor responders and women over 35 years
AUTHOR(S): D'Amato, Giuseppe; Caroppo, Ettore; Pasquadibisceglie, Annamaria; Carone, Domenico; Vitti, Angela; Vizziello, Giovanni Michele
CORPORATE SOURCE: Unita Operativa di Fisiopatologia della Riproduzione Umana, IRCCS "S. De Bellis", Castellana Grotte, Italy
SOURCE: Fertility and Sterility (2004), 81(6), 1572-1577
CODEN: FESTAS; ISSN: 0015-0282
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Objective: To evaluate the efficacy of a novel protocol of ovulation induction for poor responders. Design: Prospective, controlled, clin. study. Setting: Research institute's reproductive unit. Patient(s): One hundred forty-five infertile women, aged 27-39 years, candidates for assisted reproductive techniques (ART). Intervention(s): Before undergoing ART, 85 patients received **clomiphene** citrate, high-dose recombinant human FSH, and a delayed, multidose GnRH antagonist, whereas 60 patients underwent a standard long protocol. Main Outcome Measure(s): Estradiol levels (pg/mL), cancellation rate, oocyte retrieval, embryo score, and fertilization and pregnancy rates. Result(s): Patients undergoing the study protocol obtained lower cancellation rates (4.7% vs. 34%) and higher E2 levels (945.88 ± 173.2 pg/mL vs. 169.55 ± 45.07

pg/mL), oocyte retrieval (5.56 ± 1.13 vs. 3.36 ± 1.3), and pregnancy (22.2% vs. 15.3%) and implantation rates (13.5% vs. 7.6%) compared with those receiving the long protocol. Age neg. correlated with ovarian response in the latter, whereas the ovarian outcome results were comparable in younger (<35 yrs) and older (>35 yrs) women treated with the study protocol. Conclusion(s): The proposed protocol of ovulation induction can be usefully administered in poor responders as well as in aged woman, probably because the delayed administration of GnRH antagonist prevents its adverse effects on ovarian paracrine activity and on oocyte maturation.

IT Fertility disorders
(female; ovulation induction with delayed gonadotropin-releasing hormone antagonist combined with recombinant FSH and **clomiphene** citrate for poor responders and women over 35 yr)

IT Egg
(oocyte; ovulation induction with delayed gonadotropin-releasing hormone antagonist combined with recombinant FSH and **clomiphene** citrate for poor responders and women over 35 yr)

IT **Aging**, animal
Combination chemotherapy
Fertilization
Human
Ovulation induction
Reproduction disorders
(ovulation induction with delayed gonadotropin-releasing hormone antagonist combined with recombinant FSH and **clomiphene** citrate for poor responders and women over 35 yr)

IT 9034-40-6, Gonadotropin-releasing hormone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonist; ovulation induction with delayed gonadotropin-releasing hormone antagonist combined with recombinant FSH and **clomiphene** citrate for poor responders and women over 35 yr)

IT 50-41-9, Serophene 74381-53-6, Enantone 145672-81-7, Cetrotide 146479-72-3, Gonal F
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ovulation induction with delayed gonadotropin-releasing hormone antagonist combined with recombinant FSH and **clomiphene** citrate for poor responders and women over 35 yr)

IT 9002-61-3, Profasi
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ovulation induction with delayed gonadotropin-releasing hormone antagonist combined with recombinant FSH and **clomiphene** citrate for poor responders and women over 35 yr)

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 21 OF 160 EMBASE 

ACCESSION NUMBER: 2004159553 EMBASE

TITLE: [Impotence and decreased libido: Hypogonadism, andropause (androclise) or depression? Indications and risks of an androgen replacement therapy].
IMPUISSANCE ET BAISSE DE LA LIBIDO: HYPOGONADISME, ANDROPAUSE (ANDROCLISE) OU DEPRESSION? INDICATIONS ET RISQUES D'UN TRAITEMENT ANDROGENIQUE.

AUTHOR: Martin-Du Pan R.C.

CORPORATE SOURCE: Dr. R.C. Martin-Du Pan, 26, bd Helvetique, 1207 Geneve, Switzerland

SOURCE: Medecine et Hygiene, (17 Mar 2004) Vol. 62, No. 2474, pp. 602-607. .
Refs: 36
ISSN: 0025-6749 CODEN: MEHGAB

COUNTRY: Switzerland

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 003 Endocrinology
028 Urology and Nephrology
032 Psychiatry

037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: French
SUMMARY LANGUAGE: English; French
ENTRY DATE: Entered STN: 20040429
Last Updated on STN: 20040429

AB Hypogonadism is caracterized by low serum levels of T (< 7 nmol/l), reduced bone and muscle mass, decreased libido and erectile function. An androgenic treatment can improve these symptoms. Similar but less pronounced symptoms are also observed in **aging** men with subclinical hypogonadism (T serum levels between 9 an 12 mmol/l), which is known as andropause. Indication to a prolonged androgen treatment in andropause is controversial because of cardiovascular and prostatic risks which still need an evaluation in long term (> 3 years) studies. Depression can also be associated with decreased libido and erection together with subnormal T levels. However depression is alleviated selectively by a treatment with antidepressive drugs whereas androgens can increase the response to these drugs in some cases.

L23 ANSWER 22 OF 160 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:936925 CAPLUS
DOCUMENT NUMBER: 142:212514
TITLE: Ovulation induction in women with polycystic ovary syndrome: randomized trial of **clomiphene** citrate versus low-dose recombinant FSH as first line therapy
AUTHOR(S): Lopez, Eugenio; Gunby, Joanne; Daya, Salim; Parrilla, Juan J.; Abad, Lorenzo; Balasch, Juan
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Hospital Universitario Virgen de la Arrixaca, Murcia, Spain
SOURCE: Reproductive BioMedicine Online (2004), 9(4), 382-390
CODEN: RBOEA6; ISSN: 1472-6483
PUBLISHER: Reproductive Healthcare Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This single center randomized controlled trial was undertaken to compare the efficacy and safety of **clomiphene** citrate and low-dose recombinant FSH as first line pharmacol. therapy for anovulatory infertility associated with polycystic ovary syndrome (PCOS). Seventy-six infertile patients with PCOS were randomized to receive **clomiphene** citrate (50-150 mg/day for 5 days) (**clomiphene** citrate group, n = 38) or recombinant human FSH (FSH group, n = 38) in a chronic, low-dose, step-up protocol (daily starting dose 75 IU) for up to three consecutive cycles. Ovarian response was monitored by transvaginal ultrasonog. and human chorionic gonadotrophin (HCG) was given to trigger ovulation in all cycles with appropriate follicular development. The primary outcome measure was cumulative pregnancy after undergoing up to three treatment cycles. Secondary outcomes were cycle cancellation rate, ovulation rate per cycle, cumulative ovulation rate, pregnancy rate per cycle, incidence of OHSS, cumulative live birth rate, and multiple birth rate. One hundred and four **clomiphene** citrate cycles and 91 FSH cycles were evaluable. The relative risk and its 95% confidence interval were 1.17 (0.97-1.46) for HCG cycles with ovulation, 1.78 (0.92-3.54) for the pregnancy rate per woman, and 1.83 (0.79-4.40) for live births per woman in favor of FSH. The cumulative pregnancy rate after three treatment cycles was 43% with FSH and 24% with **clomiphene** citrate (P = 0.06). By logistic regression anal., the factors predicting ovulation included female age, serum androstenedione and use of FSH. Predictors of pregnancy were duration of infertility and use of FSH. This randomized controlled trial suggests that low-dose recombinant FSH may be an effective alternative to **clomiphene** citrate in first-line treatment for anovulatory PCOS patients. Thus, further studies, possibly multi-center, to avoid problems with patient recruitment, are warranted to confirm these results.

IT **Aging**, animal
(factors predicting ovulation included female age, serum androstenedione and use of FSH in women with polycystic ovary syndrome)
IT Fertility disorders
(female; ovulation induction in women with polycystic ovary syndrome

and randomized trial of **clomiphene** citrate (Omifin) vs. low-dose recombinant FSH (Gonal-F) as first line therapy)

IT Ovary
(follicle; ovulation induction in women with polycystic ovary syndrome and randomized trial of **clomiphene** citrate (Omifin) vs. low-dose recombinant FSH (Gonal-F) as first line therapy)

IT Human
Ovulation
Pregnancy
(ovulation induction in women with polycystic ovary syndrome and randomized trial of **clomiphene** citrate (Omifin) vs. low-dose recombinant FSH (Gonal-F) as first line therapy)

IT Ovary, disease
(polycystic; ovulation induction in women with polycystic ovary syndrome and randomized trial of **clomiphene** citrate (Omifin) vs. low-dose recombinant FSH (Gonal-F) as first line therapy)

IT 63-05-8, Androstenedione
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(factors predicting ovulation included female age, serum androstenedione and use of FSH in women with polycystic ovary syndrome)

IT 50-41-9, Omifin 146479-72-3, Gonal-F
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ovulation induction in women with polycystic ovary syndrome and randomized trial of **clomiphene** citrate (Omifin) vs. low-dose recombinant FSH (Gonal-F) as first line therapy)

IT 9002-61-3, Profasi
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ovulation induction in women with polycystic ovary syndrome and randomized trial of **clomiphene** citrate (Omifin) vs. low-dose recombinant FSH (Gonal-F) as first line therapy)

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 23 OF 160 EMBASE 

ACCESSION NUMBER: 2004508649 EMBASE

TITLE: Genetics and bioenergetics of mitochondria influencing the etiology and pharmacology of steroidal hormones.

AUTHOR: Roy D.; Parkash J.; Narayan S.

CORPORATE SOURCE: D. Roy, Environmental/Occup. Health Program, Robert Stempel Sch. of Public Health, Florida International University, 11200 S.W. 8th Street, Miami, FL 33199, United States. Droy@fiu.edu

SOURCE: Current Pharmacogenomics, (2004) Vol. 2, No. 4, pp. 379-390. .
Refs: 163
ISSN: 1570-1603 CODEN: CPUHAC

COUNTRY: Netherlands

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 003 Endocrinology
005 General Pathology and Pathological Anatomy
022 Human Genetics
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20041217
Last Updated on STN: 20041217

AB Mitochondria are important targets of steroid hormone action. The receptors for steroid hormones, including estrogen, thyroxine and glucocorticoid, are present in the mitochondria, while steroid hormone responsive elements are also found in the mitochondrial genome. The presence of the steroid hormone receptors in the mitochondria, transport of ligands to the mitochondria, sequences of hormone response elements in the mitochondrial genome, and modulation of mitochondrial encoded genes by steroid hormones support a direct action of steroid hormones on mitochondrial gene transcription. This is parallel to the primary actions

of the steroid hormones on nuclear gene transcription as a mechanism to coordinate regulation of mitochondrial biogenesis by steroid hormones. The cross-talk between the cell nucleus and the mitochondria appears to control steroid hormone-induced signaling involved in the apoptosis, proliferation, and differentiation of both normal and malignant cells. Evaluation of the defects in genetics and physiology of mitochondria, specifically in steroids hormone-related endocrine diseases in humans, suggests that several variants of human endocrine diseases, including cancer, manifest as a result of mitochondrial physiologic and metabolic compensation of genetic defects. The steroidal agents control biogenesis and maintenance of mitochondria through the crosstalk between nuclear and mitochondrial genomes. The regulation of mitochondrial transcription by steroidal hormones, presumably occurring through pathways similar to those that take place in the nucleus, opens a new way to better understand steroid hormone and vitamin action at the cellular level. Therefore, an in-depth analysis of such regulatory mechanisms is pertinent to the development of novel drugs and gene therapy strategies for the treatment of steroid hormone-dependent diseases related to mitochondrial disorders including cancer. .COPYRGT. 2004 Bentham Science Publishers Ltd.

L23 ANSWER 24 OF 160 MEDLINE on STN
ACCESSION NUMBER: 2004018729 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14715867
TITLE: Anti-Mullerian hormone serum concentrations in normoovulatory and anovulatory women of reproductive age.
AUTHOR: Laven Joop S E; Mulders Annemarie G M G J; Visser Jenny A; Themmen Axel P; De Jong Frank H; Fauser Bart C J M
CORPORATE SOURCE: Division of Reproductive Medicine, Department of Obstetrics and Gynecology, Erasmus Medical Center, Rotterdam, The Netherlands.. j.laven@erasmusmc.nl
SOURCE: The Journal of clinical endocrinology and metabolism, (2004 Jan) Vol. 89, No. 1, pp. 318-23.
Journal code: 0375362. ISSN: 0021-972X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 20040113
Last Updated on STN: 20040212
Entered Medline: 20040211

AB Anti-Mullerian hormone (AMH) concentrations correlate with the number of antral follicles as well as age and constitute an endocrine marker for ovarian **aging**. In normogonadotropic anovulatory infertile women [World Health Organization (WHO) class 2], the number of early antral follicles is usually increased. To investigate whether AMH concentrations are increased, serum levels in 128 WHO 2 women were compared with those in 41 normoovulatory premenopausal women of similar age. Serum AMH concentrations are significantly (P < 0.001) elevated in WHO 2 patients [median, 7.6 micro g/liter (range, 0.1-40.0)], compared with controls [median, 2.1 micro g/liter (0.1-7.4)]. In 106 patients presenting with polycystic ovaries (PCOs) (>/==" BORDER="0">12 follicles/ovary measuring 2-9 mm and/or an ovarian volume > 10 ml), AMH levels were elevated [9.3 micro g/liter (1.8-40.0)], compared with 22 patients without PCOs [6.4 micro g/liter (0.1-22.1)] (P < 0.0001). In WHO 2 patients, AMH concentrations correlated with features characteristic for polycystic ovary syndrome such as LH concentrations (r = 0.331; P = 0.0001), testosterone levels (r = 0.477, P = 0.0001), mean ovarian volume (r = 0.421; P = 0.0001), and the number of ovarian follicles (r = 0.308; P = 0.0001). AMH levels correlated well with age in WHO 2 patients (r = -0.248; P = 0.002) as well as in controls (r = -0.465; P = 0.005). However, the relative decline in AMH with age is less pronounced in WHO 2 patients. In a subset of patients no significant correlation was found between AMH serum concentrations and the FSH response dose, the duration of stimulation, and the total number of ampoules of FSH used. In conclusion, serum AMH concentrations are elevated in WHO 2 women, especially in those patients exhibiting PCOs. Because AMH concentrations correlated well with other clinical, endocrine, and ultrasound markers associated with polycystic ovary syndrome, AMH may be used as a marker for

the extent of the disease. A less pronounced AMH decrease over time in these women may suggest retarded ovarian **aging**. The latter hypothesis, however, should be confirmed by longitudinal studies.

L23 ANSWER 25 OF 160 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:366253 BIOSIS
DOCUMENT NUMBER: PREV200400369334
TITLE: Comparison of basal follicle-stimulating hormone versus the **clomiphene** citrate challenge test for ovarian reserve screening.
AUTHOR(S): Jain, Tarun [Reprint Author]; Soules, Michael R.; Collins, John A.
CORPORATE SOURCE: Dept Obstet and Gynecol, Univ Illinois, 820 S Wood St, Chicago, IL, 60612, USA
tjain99@yahoo.com
SOURCE: Fertility and Sterility, (July 2004) Vol. 82, No. 1, pp. 180-185. print.
ISSN: 0015-0282 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Sep 2004
Last Updated on STN: 8 Sep 2004

AB Objective: To compare the value of basal follicle-stimulating hormone (FSH) measurement vs. the **clomiphene** citrate challenge test (CCCT) in predicting the ability to achieve a pregnancy in women who are undergoing infertility treatment. Design: Meta-analysis. Setting: All studies that evaluated either basal FSH or the CCCT for determining the likelihood of pregnancy. Patient(s): Infertility population undergoing treatment, which was defined as patients undergoing ovulation induction, IUI, or in vitro fertilization (IVF). Intervention(s): None. Main Outcome Measure(s): Diagnostic test characteristics were calculated and pooled using standard methods. Inability to achieve a pregnancy with treatment was considered as the "disease." Result(s): Twelve studies on basal FSH (with 6,296 patients, mean age 33.8) and seven studies on the CCCT (with 1,352 patients, mean age 34.5) fit our criteria and were analyzed. For basal FSH and the CCCT, the sensitivities were 6.6% (95% confidence interval (CI) 5.9, 7.3%) and 25.9% (95% CI 23.0, 29.0%), respectively, and specificities were 99.6% (95% Cl 99.1, 99.9%) and 98.1% (95% Cl 96.5, 99.1%), respectively. For "disease" prevalence ranging from 40%-100%, for basal FSH and the CCCT, the positive predictive values ranged from 91.7%-100% and 90.1%-100%, respectively, and negative predictive values ranged from 61.5%-0.0% and 66.5%-0.0%, respectively. Conclusion(s): Basal FSH and the CCCT are similar in predicting the ability to achieve a clinical pregnancy in women undergoing infertility treatment. With either test, a normal result is not useful, but an abnormal result virtually confirms that pregnancy will not occur with treatment.

IT Major Concepts
**Aging**; Clinical Endocrinology (Human Medicine, Medical Sciences); Gynecology (Human Medicine, Medical Sciences); Information Studies; Methods and Techniques; Pharmacology
IT Diseases
infertility: reproductive system disease, reproductive system disease/female, reproductive system disease/male, drug therapy, therapy
Infertility (MeSH)
IT Chemicals & Biochemicals
FSH: basal, predictive value
IT Methods & Equipment
**clomiphene** citrate challenge test: clinical techniques, diagnostic techniques; meta-analysis: mathematical and computer techniques; ovarian reserve screening: clinical techniques, diagnostic techniques
IT Miscellaneous Descriptors
assisted reproductive technology; pregnancy; reproductive **aging**
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia

Organism Name
human (common): patient, female
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 9002-68-0 (FSH)

L23 ANSWER 26 OF 160 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2004217973 EMBASE
TITLE: Current controversies in testosterone testing: **Aging** and obesity.
AUTHOR: Elin R.J.; Winters S.J.
CORPORATE SOURCE: Dr. R.J. Elin, Dept. of Pathol. and Lab. Medicine, University of Louisville, School of Medicine, 512 South Hancock Street, #203, Louisville, KY 40202, United States. rjelin01@gwise.louisville.edu
SOURCE: Clinics in Laboratory Medicine, (2004) Vol. 24, No. 1, pp. 119-139. .
Refs: 96
ISSN: 0272-2712 CODEN: CLMED6
PUBLISHER IDENT.: S 0272-2712(04)00011-3
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
020 Gerontology and Geriatrics
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20040628
Last Updated on STN: 20040628
AB The interpretation of the total serum testosterone concentration is problematic because it is related directly to the serum SHBG concentration. Frequently, an estimate of the serum free testosterone concentration is obtained to better assess the clinical status of the patient. We reviewed five methods for the determination of free testosterone or a surrogate test/index and the problems with these methods. The calculated free testosterone or BAT (highly positively correlated) are recommended as the preferred tests to assess biologically-active testosterone, although interlaboratory values may differ because standards are not available. The controversies in evaluating gonadal function are illustrated by the andropause (elevated SHBG) and obese men (decreased SHBG).

L23 ANSWER 27 OF 160 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:612749 CAPLUS
DOCUMENT NUMBER: 143:453128
TITLE: Blastocyst transfer in **clomiphene** citrate/gonadotropins cycle for IVF-ET
AUTHOR(S): Nishimoto, M.; Fujino, Y.; Yamashita, N.; Miyata, S.; Sasaki, M.; Yokoyama, A.; Kawashima, K.
CORPORATE SOURCE: Towako Reproduction Center, Osaka, 564-0051, Japan
SOURCE: International Congress Series (2004), 1271(Research Papers in Fertility and Reproductive Medicine), 105-107
CODEN: EXMDA4; ISSN: 0531-5131
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Total of 205 cycles were performed IVF and single blastocyst transfer under the control with **clomiphene** citrate and gonadotropins. Of the 205 cycles, 44 resulted in clin. pregnancy. In older patients with good embryos, the yield of blastocyst formation is reassuring (35.5%) but their pregnancy rate (11.1%) remains lower than that of younger patients (40.0-34.5%). We conclude that IVF using **clomiphene** citrate and gonadotropins is a possible alternative to current standard protocol with the controlled ovarian hyperstimulation, from the low-risk profile and easy repeatability of this protocol.
IT **Aging**, animal

Human
In vitro fertilization
Ovulation induction
(blastocyst transfer in **clomiphene** citrate/gonadotropins cycle for IVF-ET)
IT Gonadotropins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(blastocyst transfer in **clomiphene** citrate/gonadotropins cycle for IVF-ET)
IT Embryo, animal
(blastocyst; blastocyst transfer in **clomiphene** citrate/gonadotropins cycle for IVF-ET)
IT Fertility
(female; blastocyst transfer in **clomiphene** citrate/gonadotropins cycle for IVF-ET)
IT 50-41-9, **Clomiphene** Citrate 61489-71-2, Humegon 868948-10-1, Spruque
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(blastocyst transfer in **clomiphene** citrate/gonadotropins cycle for IVF-ET)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 28 OF 160 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:30753 BIOSIS
DOCUMENT NUMBER: PREV200500031171
TITLE: **Aging** and infertility in women.
AUTHOR(S): Practice Comm Amer Soc Reprod Med [Reprint Author]
SOURCE: Fertility and Sterility, (September 2004) Vol. 82, No. Suppl. 1, pp. S102-S106. print.
ISSN: 0015-0282 (ISSN print).
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Jan 2005
Last Updated on STN: 12 Jan 2005
IT Major Concepts
**Aging**; Gynecology (Human Medicine, Medical Sciences); Methods and Techniques
IT Parts, Structures, & Systems of Organisms
oocyte: reproductive system; ovary: reproductive system; semen: reproductive system, quality; sperm: reproductive system, morphology, motility
IT Diseases
infertility: reproductive system disease, reproductive system disease/female, reproductive system disease/male, diagnosis, drug therapy, etiology
Infertility (MeSH)
IT Diseases
spontaneous abortion: reproductive system disease/female
Abortion, Spontaneous (MeSH)
IT Chemicals & Biochemicals
**clomiphene** citrate: fertility-drug
IT Methods & Equipment
assisted reproduction: clinical techniques; in vitro fertilization: clinical techniques; sonography: clinical techniques, diagnostic techniques
IT Miscellaneous Descriptors
**aging**; menopause; pregnancy rate; reproductive age
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human (common): adult, female, male
Taxa Notes

Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 50-41-9 (**clomiphene** citrate)

L23 ANSWER 29 OF 160 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2004028212 EMBASE
TITLE: Off to a good start: The influence of pre- and periconceptional exposures, parental fertility, and nutrition on children's health.
AUTHOR: Chapin R.E.; Robbins W.A.; Schieve L.A.; Sweeney A.M.; Tabacova S.A.; Tomashek K.M.
CORPORATE SOURCE: R. Chapin, Pfizer Global Research/Development, Safety Sciences, Eastern Point Road, Groton, CT 06340, United States. robert_e_chapin@groton.pfizer.com
SOURCE: Environmental Health Perspectives, (2004) Vol. 112, No. 1, pp. 69-78. .
Refs: 212
ISSN: 0091-6765 CODEN: EVHPAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
010 Obstetrics and Gynecology
017 Public Health, Social Medicine and Epidemiology
037 Drug Literature Index
038 Adverse Reactions Titles
046 Environmental Health and Pollution Control
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20040129
Last Updated on STN: 20040129
AB The scientific community is developing a compelling body of evidence that shows the importance of the in utero environment (including chemical and hormonal levels) to the ultimate health of the child and even of the **aging** adult. This article summarizes the evidence that shows this impact begins with conception. Only a full life-cycle evaluation will help us understand these impacts, and only such an understanding will produce logically prioritized mitigation strategies to address the greatest threats first. Clearly, the time for analysis begins when the next generation is but a twinkle in the eye.

L23 ANSWER 30 OF 160 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2004:789574 CAPLUS
DOCUMENT NUMBER: 141:360752
TITLE: Inhibins and adult ovarian function
AUTHOR(S): Laven, J. S. E.; Fauser, B. C. J. M.
CORPORATE SOURCE: Department of Obstetrics and Gynaecology, Division of Reproductive Medicine, Erasmus Medical Center, Rotterdam, 3015 GD, Neth.
SOURCE: Molecular and Cellular Endocrinology (2004), 225(1-2), 37-44
CODEN: MCEND6; ISSN: 0303-7207
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Inhibin B is predominantly produced by early healthy antral follicles during the luteo-follicular transition of the menstrual cycle. High inhibin B concns. during the early follicular phase are responsible for the decline in FSH serum levels closing the FSH window and assuring single dominant follicle selection in the human. Early follicular phase inhibin B levels decrease over time, reflecting the recruitment of a diminished cohort of follicles with ovarian **aging**. Hence, inhibin B is a predictor of poor response in IVF. In patients with PCOS inhibin B levels (potentially representing the number of healthy, early antral follicles) may be associated with the severity of ovarian dysfunction and consequently may predict ovulation induction outcome. However, inhibin B levels are normal in most PCOS patients suggesting a normal number of healthy follicles despite an increase in overall follicle number Recent findings indicate that initial inhibin B concns. can not predict the outcome of ovulation induction by either **clomiphene** citrate or

FSH. Finally, inhibin B levels decrease over time in PCOS.
IT **Aging**, animal
(effect on ovarian function; inhibins and normal, **aging** and pathol. ovarian function)
IT Human
Ovarian cycle
Ovary
Ovary, disease
(inhibins and normal, **aging** and pathol. ovarian function)
IT 57285-09-3, Inhibin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibins and normal, **aging** and pathol. ovarian function)
REFERENCE COUNT: 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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(FILE 'HOME' ENTERED AT 14:42:11 ON 01 MAR 2006)

FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE' ENTERED AT 14:42:45 ON 01 MAR 2006
L1 1613 S 79838-56-5/RN OR 57049-00-0/RN OR 39729-47-0/RN OR 15690-57-0
L2 18503 S CLOMIPHENE OR ENCLOMIFENE OR ENCLOMIPHENE TRANS-CLOMIFENE OR
L3 299 S CIS-CLOMIPHENE OR ZUCLOMID OR ZUCLOMIPHENE
L4 6 S ENCLOMID OR TRANS-CLOMIPHEN
L5 99 S ENCLOMID OR TRANS-CLOMIPHENE
L6 300 S L3 OR CIS-CLOMIFENE
L7 359 S L3 OR ZUCLOMIFENE
L8 31489 S TESTESTERONE OR 17-HYDROXY-5ALPHA-ANDROST-1-EN-3-ONE OR 1-T
L9 3847772 S WASTING OR SLUGGISH OR MOOD OR FEELING OR ENERGY OR STAMINA O
L10 138 S L9 AND L2
L11 21 S L9 AND L7
L12 1 S L9 AND L5
L13 94 DUP REM L10 (44 DUPLICATES REMOVED)
L14 94 FOCUS L13 1-
L15 620699 S CACHEXIA OR AGING OR MYOPATHIES OR NEUROMYOPATHY OR MYOPATHY
L16 707670 S BRACHIAL PLEXOPATHY, DIABETIC AMYOTROPHY OR DENERVATION OR HI
L17 1319441 S L15 OR L16
L18 200 S L17 AND L2
L19 13 S L18 AND L7
L20 1 S L18 AND L5
L21 18607 S CLOMIPHENE OR ENCLOMIFENE OR ENCLOMIPHENE OR TRANS-CLOMIFENE
L22 200 S L21 AND L17
L23 160 DUP REM L22 (40 DUPLICATES REMOVED)
L24 160 FOCUS L23 1-
L25 13 DUP REM L19 (0 DUPLICATES REMOVED)
L26 13 FOCUS L25 1-

=> s l23 not aging
L27 23 L23 NOT AGING

=> d ibib abs it 1-23

L27 ANSWER 1 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:100738 CAPLUS
TITLE: Novel dosage form comprising modified-release and immediate-release active ingredients
INVENTOR(S): Vaya, Navin; Karan, Rajesh Singh; Sadanand, Sunil; Gupta, Vinod Kumar
PATENT ASSIGNEE(S): India
SOURCE: U.S. Pat. Appl. Publ., 49 pp., Cont.-in-part of U.S. Ser. No. 630,446.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

| | | | | | |
|---|---|---|---|---|---|
| US 2006024365 | A1 | 20060202 | US 2005-134633 | | 20050519 |
| US 2004096499 | A1 | 20040520 | US 2003-630446 | | 20030729 |
| PRIORITY APPLN. INFO.: | | | IN 2002-MU697 | A | 20020805 |
| | | | IN 2002-MU699 | A | 20020805 |
| | | | IN 2003-MU80 | A | 20030122 |
| | | | IN 2003-MU82 | A | 20030122 |
| | | | US 2003-630446 | A2 | 20030729 |

AB A dosage form comprising of a high dose, high solubility active ingredient as modified release and a low dose active ingredient as immediate release where the weight ratio of immediate release active ingredient and modified release active ingredient is from 1:10 to 1:15000 and the weight of modified release active ingredient per unit is from 500 mg to 1500 mg; a process for preparing the dosage form. Tablets containing 10 mg sodium pravastatin and 1000 mg niacin were prepared The release of sodium pravastatin after 24 h was 67.7%, and the release of niacin after 1 h was 84.1%.

IT tRNA
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(2-(diethylamino)ethanol complexes; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Fatty acids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C14-18, C14-18-alkyl esters; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Alcohols
Glycerides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C16-18; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Antihistamines
(H2; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Histamine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(H2; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Canarypox virus
(IL-2; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Natural products, pharmaceutical
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Kutkin; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Glutamate antagonists
(NMDA antagonists; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Bone, disease
(Paget's, drugs for treatment of; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Monoglycerides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(acetates; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Estrogen receptors
Estrogens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonists; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Nervous system, disease
(**amyotrophic lateral sclerosis**, drugs for treatment of; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Hormones, animal
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anabolic steroids; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Polyamines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(analogs; novel dosage form comprising modified-release and

immediate-release active ingredients)
IT Heart, disease
(angina pectoris, unstable, drugs for treatment of; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Antirheumatic agents
(antagonist; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Antiarteriosclerotics
(antiatherosclerotics; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Antitumor agents
(antineoplastons; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Natural products, pharmaceutical
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(belladonna; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Enzymes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cell-lytic; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Ischemia, disease
(cerebral, drugs for treatment of; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Porphyrins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chlorins, benzo-; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Porphyrins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chlorins; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Tannins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compds. with 8-L-argininevasopressin; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Estrogens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugated; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Quinones
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclopentanthraquinones; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Natural products, pharmaceutical
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(digitalis; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Gastrointestinal motility
(effectors; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Fatty acids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(esters; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Placenta
(extract, Laennec; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Rhus diversiloba
(extract; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Alcohols
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fatty; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(follicle regulatory; novel dosage form comprising modified-release and immediate-release active ingredients)

IT Hair preparations
(growth stimulants; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Mucopolysaccharides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heparinoids; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Castor oil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrogenated; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Peptides
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(immunostimulant; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Acne
Bone resorption inhibitors
Cartilage
Signal transduction, biological
Thyroid gland
Translation, genetic
Ulcer
(inhibitors; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Gastric acid
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Brain, disease
(ischemia, drugs for treatment of; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Gonadotropins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(memopausal; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Hydrocarbon waxes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microcryst.; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Double stranded RNA
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mismatched; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mumps skin test; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Eye
Nervous system agents
(mydriatics; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Decongestants
(nasal; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Cytoprotective agents
(neuroprotective; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Agranulocytosis
(neutropenia, inhibitors; novel dosage form comprising modified-release and immediate-release active ingredients)
IT 5-HT antagonists
Adrenoceptor agonists
Adrenoceptor antagonists
Allergy inhibitors
Analgesics
Anesthetics
Angiogenesis inhibitors
Antiandrogens
Antianginal agents

Antiarthritics
Antiasthmatics
Anticholesteremic agents
Anticoagulants
Antidiabetic agents
Antiemetics
Antiestrogens
Antihypertensives
Antioxidants
Antitumor agents
Antiviral agents
Appetite depressants
Beeswax
Bronchodilators
Cholinergic agonists
Cytotoxic agents
Diphtheria
Diuretics
Dopamine agonists
Expectorants
Fibrinolytics
Hemostatics
Hypnotics and Sedatives
Hypolipemic agents
Imaging agents
Immunomodulators
Immunostimulants
Immunosuppressants
Nervous system stimulants
Neuromuscular blocking agents
Ozocerite
Parasiticides
Pituitary gland
Platelet aggregation inhibitors
Psychotropics
Radical scavengers
Radioactive substances
Rauvolfia serpentina
Tranquilizers
Vasoconstrictors
Vasodilators
Wound healing
(novel dosage form comprising modified-release and immediate-release active ingredients)

IT Acrylic polymers
Amino acids
Antisense oligonucleotides
Carnauba wax
Corticosteroids
Estrogens
Fibrinogens
Glucocorticoids
Gonadotropins
Hormones, animal
Interferons
Interleukins
Neuregulin 1
Oligonucleotides
Pentosans
Ribozymes
Stem cell factor
Steroids
Taxanes
Thyroid hormones
Tuberculin
Waxes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release active ingredients)

IT Proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reticulon; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Oligonucleotides
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sense; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Muscle relaxants
(spasmolytics; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Protamines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sulfates; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Glycosaminoglycans
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthetic; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Drug delivery systems
(tablets, compressed; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Drug delivery systems
(tablets, immediate release; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Drug delivery systems
(tablets, sustained-release; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Drug delivery systems
(tablets; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Dyes
(tellurapyrylium; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(trichohyalins; novel dosage form comprising modified-release and immediate-release active ingredients)
IT Cytotoxic agents
(tyrphostins; novel dosage form comprising modified-release and immediate-release active ingredients)
IT 249886-47-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CLX 0921; novel dosage form comprising modified-release and immediate-release active ingredients)
IT 151763-64-3
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Capromab; novel dosage form comprising modified-release and immediate-release active ingredients)
IT 9034-40-6, LHRH
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(agonists; novel dosage form comprising modified-release and immediate-release active ingredients)
IT 52-39-1, Aldosterone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonist; novel dosage form comprising modified-release and immediate-release active ingredients)
IT 65154-06-5, Platelet activating factor
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antagonists; novel dosage form comprising modified-release and immediate-release active ingredients)
IT 50-99-7, D-Glucose
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(blood, regulators; novel dosage form comprising modified-release and immediate-release active ingredients)
IT 676559-96-9, Aethacizin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ethacizin; novel dosage form comprising modified-release and immediate-release active ingredients)

IT 50-67-9, Serotonin 70-18-8, Glutathione 9040-48-6, Gelatinase
52660-18-1, Casein kinase 79955-99-0, Stromelysin 120178-12-3,
Telomerase 141256-52-2, Matrilysin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; novel dosage form comprising modified-release and
immediate-release active ingredients)

IT 9002-17-9, Xanthine oxidase 9013-05-2, Phosphatase 106096-93-9, Bfgf
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors; novel dosage form comprising modified-release and
immediate-release active ingredients)

IT 50-02-2, Dexamethasone 50-04-4, Cortisone acetate 50-06-6,
Phenobarbital 50-12-4, Mephenytoin 50-13-5, Meperidine hydrochloride
50-18-0, Cyclophosphamide 50-19-1, Hydroxyphenamate 50-23-7,
Hydrocortisone 50-24-8, Prednisolone 50-27-1, Estriol 50-28-2,
Estra-1,3,5(10)-triene-3,17-diol (17β)- 50-33-9, Phenylbutazone
50-34-0, Propantheline bromide 50-35-1, Thalidomide 50-36-2, Cocaine
50-52-2, Thioridazine 50-53-3, Chlorpromazine 50-55-5, Reserpine
50-56-6, Oxytocin 50-57-7, Lypressin 50-58-8, Phendimetrazine tartrate
50-59-9, Cephaloridine 50-65-7, Niclosamide 50-76-0, Dactinomycin
50-78-2, Aspirin 50-91-9, Floxuridine 51-05-8, Procaine hydrochloride
51-15-0, Pralidoxime chloride 51-21-8, Fluorouracil 51-30-9,
Isoproterenol hydrochloride 51-40-1, Norepinephrine bitartrate
51-43-4, Epinephrine 51-52-5, Propylthiouracil 51-55-8, Atropine
51-56-9, Homatropine hydrobromide 51-57-0, Methamphetamine hydrochloride
51-64-9, Dextroamphetamine 51-83-2, Carbachol 52-01-7, Spironolactone
52-24-4, Thiotepa 52-49-3, Trihexyphenidyl hydrochloride 52-68-6,
Metrifonate 52-76-6, Lynestrenol 52-86-8, Haloperidol 52-88-0,
Methylatropine nitrate 52-89-1, Cysteine hydrochloride 53-03-2,
Prednisone 53-16-7D, Estrone, esters 53-19-0, Mitotane 53-34-9,
Fluprednisolone 53-39-4, Oxandrolone 53-43-0, Dehydroepiandrosterone
53-60-1, Promazine hydrochloride 53-73-6, Angiotensin amide 53-79-2,
Puromycin 53-84-9, Nadide 53-86-1, Indometacin 54-03-5, Hexobendine
54-05-7, Chloroquine 54-21-7, Sodium salicylate 54-31-9, Furosemide
54-35-3, Penicillingprocaine 54-36-4, Metyrapone 54-42-2, Idoxuridine
54-64-8, Thimerosal 54-84-2, Cinanserin hydrochloride 54-85-3,
Isoniazid 54-91-1, Pipobroman 55-03-8, Levothyroxine sodium 55-06-1,
Liothyronine sodium 55-63-0, Nitroglycerin 55-86-7, Mechlorethamine
hydrochloride 55-91-4, Isoflurophate 55-98-1, Busulfan 56-45-1,
Serine 56-47-3, Desoxycorticosterone acetate 56-53-1,
Diethylstilbestrol 56-59-7, Felypressin 56-75-7, Chloramphenicol
56-84-8, Aspartic acid 56-87-1, Lysine 56-89-3, Cystine 56-94-0,
Demecarium bromide 57-13-6, Urea 57-41-0, Phenytoin 57-47-6,
Physostigmine 57-53-4, Meprobamate 57-63-6, Ethinyl estradiol
57-65-8, Thyromedan hydrochloride 57-66-9, Probenecid 57-68-1,
Sulfamethazine 57-83-0, Progesterone 57-91-0, 17-α Estradiol
57-94-3, Tubocurarine chloride 57-96-5, Sulfinpyrazone 58-08-2,
Caffeine 58-14-0, Pyrimethamine 58-18-4, Methyltestosterone 58-22-0,
Testosterone 58-25-3, Chlordiazepoxide 58-28-6, Desipramine
hydrochloride 58-32-2, Dipyridamole 58-33-3, Promethazine
hydrochloride 58-38-8, Prochlorperazine 58-39-9, Perphenazine
58-54-8, Ethacrynic acid 58-55-9, Theophylline 58-71-9, Cephalothin
sodium 58-86-6, Xylose 58-93-5, Hydrochlorothiazide 58-94-6,
Chlorothiazide 59-05-2, Methotrexate 59-30-3, Folic acid 59-33-6,
Pyrilamine maleate 59-52-9, Dimercaprol 59-63-2, Isocarboxazid
59-67-6, Niacin 59-87-0, Nitrofurazone 59-92-7, Levodopa 59-97-2,
Tolazoline hydrochloride 60-13-9, Amphetamine sulfate 60-18-4,
Tyrosine 60-23-1, Cysteamine 60-29-7, Ether 60-45-7, Fenimide
60-54-8, Tetracycline 60-56-0, Methimazole 60-80-0, Antipyrine
60-99-1, Methotrimeprazine 61-25-6, Papaverine hydrochloride 61-56-3,
Sulthiame 61-57-4, Niridazole 61-68-7, Mefenamic acid 61-73-4,
Methylene blue 61-75-6, Bretylium tosylate 61-76-7, Phenylephrine
hydrochloride 61-90-5, Leucine 62-51-1, Methacholine chloride
62-68-0, Proadifen hydrochloride 62-73-7, Dichlorvos 62-90-8,
Nandrolone phenpropionate 63-05-8, Androstenedione 63-12-7,
Benzquinamide 63-39-8, Uridine triphosphate 63-45-6, Primaquine
phosphate 63-68-3, Methionine 63-89-8, Colfosceril palmitate
63-91-2, Phenylalanine 63-92-3, Phenoxybenzamine hydrochloride
63-98-9, Phenacemide 64-31-3, Morphine sulfate 64-43-7, Amobarbital
sodium 64-55-1, Mebutamate 64-77-7, Tolbutamide 64-86-8, Colchicine

65-28-1, Phentolamine mesylate 65-29-2, Gallamine triethiodide
65-45-2, Salicylamide 66-75-1, Uracil mustard 66-76-2, Dicumarol
66-81-9, Cycloheximide 67-20-9, Nitrofurantoin 67-43-6, Pentetic acid
67-45-8, Furazolidone 67-63-0, Isopropyl alcohol 67-68-5, Dimethyl
sulfoxide 67-73-2, Fluocinolone acetonide 67-92-5, Dicyclomine
hydrochloride 67-95-8, Quingestrone 67-96-9, Dihydrotachysterol
68-22-4, Norethindrone 68-23-5, Norethynodrel 68-35-9, Sulfadiazine
68-41-7, Cycloserine 68-89-3, Dipyrone 68-91-7, Trimethaphan camsylate
68-96-2, 17 hydroxy progesterone 69-44-3, Amodiaquine hydrochloride
69-53-4, Ampicillin 69-57-8, Penicillingsodium 69-65-8, Mannitol
69-72-7, Salicylic acid 69-74-9, Cytarabine hydrochloride 70-00-8,
Trifluridine 70-10-0, Ticlatone 70-30-4, Hexachlorophene 71-00-1,
Histidine 71-27-2, Succinylcholine chloride 71-58-9,
Medroxyprogesterone acetate 71-63-6, Digitoxin 71-68-1, Hydromorphone
hydrochloride 71-73-8, Thiopental sodium 71-81-8, Isopropamide iodide
72-18-4, Valine 72-19-5, Threonine 72-33-3, Mestranol 72-44-6,
Methaqualone 73-09-6, Etozolin 73-22-3, Tryptophan 73-31-4,
Melatonin 73-32-5, Isoleucine 73-48-3, Bendroflumethiazide 74-79-3,
Arginine 75-00-3, Ethyl chloride 75-19-4, Cyclopropane 76-38-0,
Methoxyflurane 76-42-6, Oxycodone 76-43-7, Fluoxymesterone 76-57-3,
Codeine 76-73-3, Secobarbital 76-74-4, Pentobarbital 76-90-4,
Mepenzolate bromide 77-21-4, Glutethimide 77-26-9, Butalbital
77-27-0, Thiamylal 77-36-1, Chlorthalidone 77-41-8, Methsuximide
77-46-3, Acedapsone 77-67-8, Ethosuximide 77-86-1, Trometamol
78-11-5, Pentaerythritol tetranitrate 78-44-4, Carisoprodol 79-09-4,
Propionic acid 79-17-4, Pimagedine 79-57-2, Oxytetracycline 79-64-1,
Dimethisterone 80-08-0, Dapsone 80-50-2, Anisotropine methylbromide
81-04-9, 1,5-Naphthalenedisulfonic acid 81-13-0, Dexpanthenol 81-23-2,
Dehydrocholic acid 81-54-9, Purpurin 82-92-8, Cyclizine 83-43-2,
Methylprednisolone 83-73-8, Iodoquinol 83-74-9, Ibogaine 84-17-3,
Dienestrol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release
active ingredients)

IT 85-79-0, Dibucaine 86-13-5, Benztropine 86-34-0, Phensuximide
86-35-1, Ethotoin 86-42-0, Amodiaquine 87-08-1, Penicillin V
87-90-1, Symclosene 89-25-8, Edaravone 89-57-6, Mesalamine 90-01-7,
Salicyl alcohol 90-03-9, Mercufenol chloride 90-33-5, Hymecromone
90-86-8, Cinnamedrine 91-33-8, Benzthiazide 92-13-7, Pilocarpine
93-23-2, Lauryl isoquinolinium bromide 94-09-7, Benzocaine 94-12-2,
Risocaine 94-14-4, Isobutamben 94-20-2, Chloropropamide 94-24-6,
Tetracaine 94-25-7, Butamben 94-36-0, Benzoyl peroxide 95-25-0,
Chlorzoxazone 96-82-2 96-83-3, Iopanoic acid 97-24-5, Fenticlor
97-53-0, Eugenol 97-77-8, Disulfiram 98-72-6, Nitarsone 98-96-4,
Pyrazinamide 99-66-1, Valproic acid 99-79-6, Iophendylate 100-33-4,
Pentamidine 100-55-0, Nicotinyl alcohol 100-97-0, Methenamine
101-26-8, Pyridostigmine bromide 101-31-5, Hyoscyamine 101-40-6,
Propylhexedrine 102-71-6, Trolamine 102-76-1, Triacetin 103-90-2,
Paracetamol 104-31-4, Benzonatate 106-48-9 108-46-3, Resorcinol
110-85-0, Piperazine 112-24-3, Trientine 112-38-9, Undecylenic acid
112-72-1, 1-Tetradecanol 112-92-5, Stearyl [alcohol;] 113-18-8,
Ethchlorvynol 113-52-0, Imipramine hydrochloride 113-59-7,
Chlorprothixene 113-79-1D, Argipressin, hcompds. with tannate
113-92-8, Chlorpheniramine maleate 113-98-4, Penicillingpotassium
114-07-8, Erythromycin 114-49-8, Scopolamine hydrobromide 114-70-5,
Sodium phenylacetate 114-80-7, Neostigmine bromide 114-85-2,
Bethanidine sulfate 114-86-3, Phenformin 114-90-9, Obidoxime chloride
115-02-6, Azaserine 115-38-8, Mephobarbital 116-38-1, Edrophonium
chloride 117-96-4, Diatrizoic acid 118-68-3, Etryptamine acetate
120-29-6D, Tropine, esters 120-97-8, Dichlorphenamide 121-19-7,
Roxarsone 121-54-0, Benzethonium chloride 121-81-3, Nitromide
122-09-8, Phentermine 122-16-7, Sulfanitran 122-18-9, Cetalkonium
chloride 122-32-7D, Triolein, iodo derivs., iodine-125 and iodine 131
122-79-2, Phenylacetate 123-03-5, Cetylpyridinium chloride 123-63-7,
Paraldehyde 123-99-9, Azelaic acid 124-07-2, Octanoic acid 124-43-6,
Carbamide peroxide 124-72-1, Teflurane 124-94-7, Triamcinolone
125-33-7, Primidone 125-40-6, Butabarbital 125-45-1, Azetepa
125-71-3, Dextromethorphan 125-72-4, Levorphanol tartrate 126-07-8,
Griseofulvin 126-22-7, Butonate 126-27-2, Oxethazaine 127-07-1,

Hydroxyurea 127-33-3, Demeclocycline 127-48-0, Trimethadione
127-69-5, Sulfisoxazole 127-71-9, Sulfabenzamide 127-77-5, Sulfabenz
127-79-7, Sulfamerazine 128-13-2, Ursodiol 128-62-1, Noscapine
129-06-6, Coumadin 129-20-4, Oxyphenbutazone 129-49-7, Methysergide
maleate 129-51-1, Ergonovine maleate 129-74-8, Buclizine hydrochloride
130-16-5, Cloxyquin 130-26-7, Clioquinol 130-81-4, Quindonium bromide
131-49-7, Diatrizoate meglumine 132-17-2, Benztropine mesylate
132-35-4, Proxazole citrate 132-65-0, Dibenzothiophene 132-69-4,
Benzydamine hydrochloride 132-92-3, Methicillin sodium 132-98-9,
Penicillinvpotassium 133-11-9, Phenyl aminosalicylate 133-58-4,
Nitromersol 133-67-5, Trichlormethiazide 134-80-5, Diethylpropion
hydrochloride 135-07-9, Methyclothiazide 135-09-1, Hydroflumethiazide
136-40-3, Phenazopyridine hydrochloride 136-77-6, Hexylresorcinol
137-26-8, Thiram 137-53-1, Dextrothyroxine sodium 137-58-6, Lidocaine
138-39-6, Mafenide 143-67-9, Vinblastine sulfate 143-71-5, Hydrocodone
bitartrate 144-14-9, Anileridine 144-80-9, Sulfacetamide 144-82-1,
Sulfamethizole 145-63-1, Suramin 146-22-5, Nitrazepam 146-54-3,
Trifluprom azine 147-85-3, Proline 147-94-4, Cytarabine 148-79-8,
Thiabendazole 148-82-3, Melphalan 149-32-6, Erythritol 151-67-7,
Halothane 152-11-4, Verapamil hydrochloride 152-43-2, Quinestrol
152-47-6, Sulfalene 152-58-9, Cortodoxone 152-97-6, Fluocortolone
153-87-7, Oxypertine 154-21-2, Lincomycin 154-41-6,
Phenylpropanolamine hydrochloride 154-42-7, Thioguanine 154-68-7,
Antazoline phosphate 154-69-8, Tripelennamine hydrochloride 154-93-8,
Carmustine 156-51-4, Phenelzine sulfate 271-95-4, 1,2-Benzisoxazole
297-76-7, Ethynodiol diacetate 298-46-4, Carbamazepine 298-57-7,
Cinnarizine 298-59-9, Methylphenidate hydrochloride 299-39-8,
Sparteine sulfate 299-42-3, Ephedrine 302-22-7, Chlormadinone acetate
302-49-8, Uredepa 302-79-4, Tretinoin 303-53-7, Cyclobenzaprine
304-20-1, Hydralazine hydrochloride 304-55-2, Succimer 304-84-7,
Ethamivan 305-03-3, Chlorambucil 306-07-0, Pargyline hydrochloride
306-21-8, Hydroxyamphetamine hydrobromide 309-36-4, Methohexital sodium
314-19-2, Apomorphine hydrochloride 315-80-0, Dibenzepin hydrochloride
316-42-7, Emetine hydrochloride 317-52-2, Hexafluorenium bromide
318-98-9, Propranolol hydrochloride 319-89-1, Tetroquinone 320-67-2,
Azacitidine 322-35-0, Benserazide 326-43-2, Phenyramidol hydrochloride
329-65-7, Racepinephrine 333-36-8, Flurothyl 338-98-7, Isoflupredone
acetate 339-72-0, Levcycloserine 340-57-8, Mecloqualone 345-78-8,
Pseudoephedrine hydrochloride 346-18-9, Polythiazide 356-12-7,
Fluocinonide 357-07-3, Oxymorphone hydrochloride 357-70-0, Galantamine
359-83-1, Pentazocine 361-37-5, Methysergide 362-29-8, Propiomazine
363-20-2, Tricetamide 363-24-6, Dinoprostone 364-62-5, Metoclopramide
364-98-7, Diazoxide 366-70-1, Procarbazine hydrochloride 378-44-9,
Betamethasone 379-79-3, Ergotamine tartrate 382-67-2, Desoximetasone
389-08-2, Nalidixic acid 390-64-7, Prenylamine 396-01-0, Triamterene
404-82-0, Fenfluramine hydrochloride 404-86-4, Capsaicin 406-90-6,
Fluroxene 423-55-2, Perflubron 424-89-5, Clomegestone acetate
426-13-1, Fluorometholone 434-05-9, Methenolone acetate 434-07-1,
Oxymetholone 435-97-2, Phenprocoumon 437-74-1, Xanthinol niacinate
439-14-5, Diazepam 440-17-5, Trifluoperazine hydrochloride 443-48-1,
Metronidazole 446-86-6, Azathioprine 451-71-8, Glyhexamide 459-86-9,
Mitoguazone 465-65-6, Naloxone 466-06-8, Proscillaridin 467-22-1,
Carbiphene hydrochloride 472-15-1, Betulinic acid 474-25-9, Chenodiol
474-58-8, Sitogluside 474-86-2, Equilin 476-70-0, Boldine 480-30-8,
Dichloralphenazone 480-39-7, Pinocembrin 483-63-6, Crotamiton
486-56-6, Cotinine 486-66-8, Daidzein 501-75-7
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release
active ingredients)

IT 502-54-5, Monoctanoin 502-85-2, Sodium oxybate 503-49-1, Meglutol
504-24-5, Fampridine 506-26-3, Gamolenic acid 509-74-0, Methadyl
acetate 511-13-7, Chlophedianol hydrochloride 513-10-0, Echothiophate
iodide 514-36-3, Fludrocortisone acetate 514-65-8, Biperiden
517-09-9, Equilenin 518-28-5, Podofilox 520-85-4, Medroxyprogesterone
521-18-6, Dihydrotestosterone 522-48-5, Tetrahydrozoline hydrochloride
523-87-5, Dimenhydrinate 524-83-4, Ethybenztropine 525-26-8,
Cloperidone hydrochloride 527-75-3, Berythromycin 528-43-8, Magnolol
528-53-0, Delphinidin 528-96-1, Benzoylpas calcium 530-08-5,
Isoetharine 530-78-9, Flufenamic acid 532-03-6, Methocarbamol

533-45-9, Clomethiazole 536-33-4, Ethionamide 536-59-4, Perillyl alcohol 536-93-6, Eucatropine hydrochloride 538-23-8, Tricaprylin 541-15-1, Levocarnitine 541-79-7, Carbocloral 543-82-8, Octodrine 545-80-2, Poldine methylsulfate 547-81-9, 16-Epiestriol 548-04-9, Hypericin 548-57-2, Lucanthone hydrochloride 548-62-9, Gentian violet 548-68-5, Thiphenamil hydrochloride 549-18-8, Amitriptyline hydrochloride 550-70-9, Triprolidine hydrochloride 550-83-4, Propoxycaine hydrochloride 550-99-2, Naphazoline hydrochloride 551-11-1, Cyclosin 551-48-4, Guanoclor sulfate 552-94-3, Salsalate 554-57-4, Methazolamide 554-92-7, Trimethobenzamide hydrochloride 555-30-6, Methyldopa 555-43-1, Tristearin 555-44-2, Tripalmitin 555-65-7, Brocresine 555-84-0, Nifuradene 557-08-4, Zinc undecylenate 566-48-3, Formestane 569-57-3, Chlorotrianisene 578-95-0D, Acridone, imidazo derivs. 579-56-6, Isoxsuprine hydrochloride 581-88-4, Debrisoquin sulfate 585-86-4, Lactitol 587-61-1, Propyliodone 590-63-6, Bethanechol chloride 595-33-5, Megestrol acetate 596-51-0, Glycopyrrolate 599-79-1, Sulfasalazine 604-75-1, Oxazepam 606-05-3, Pyrabrom 609-78-9, Cycloguanil pamoate 614-39-1, Procainamide hydrochloride 630-56-8, Hydroxyprogesterone caproate 630-93-3, Dilantin 631-06-1, Dexoxadrol hydrochloride 632-00-8, Sulfasomizole 632-99-5, Fuchsin 635-41-6, Trimetozine 636-54-4, Clopamide 637-07-0, Clofibrate 637-58-1, Pramoxine hydrochloride 638-23-3, Carbocysteine 638-94-8, Desonide 645-43-2, Guanethidine monosulfate 646-08-2, β-Alethine 651-06-9, Sulfameter 652-67-5, Isosorbide 653-03-2, Butaperazine 655-05-0, Thozalinone 655-35-6, Chromonar hydrochloride 657-24-9, Metformin 672-87-7, Metyrosine 679-90-3, Roflurane 692-13-7, Buformin 695-53-4, Dimethadione 720-76-3, Fluminorex 723-46-6, Sulfamethoxazole 729-99-7, Sulfamoxole 735-52-4, Cetophenicol 738-70-5, Trimethoprim 739-71-9, Trimipramine 742-20-1, Cyclopenthiazide 747-36-4, Hydroxychloroquine sulfate 749-02-0, Spiperone 749-13-3, Trifluperidol 751-94-0, Fusidate sodium 751-97-3, Rolitetracycline 773-76-2, Chloroxine 777-11-7, Haloprogin 797-63-7, Levonorgestrel 801-52-5, Porfiromycin 804-63-7, Quinine sulfate 808-26-4, Sancycline 811-97-2, Norflurane 826-39-1, Mecamylamine hydrochloride 829-74-3, Levonordefrin 846-49-1, Lorazepam 846-50-4, Temazepam 847-25-6, Racephenicol 848-75-9, Lormetazepam 852-19-7, Sulfazamet 852-42-6, Guaiapate 860-22-0 881-17-4 886-38-4, Diphencyprone 886-74-8, Chlorphenesin carbamate 894-71-3, Nortriptyline hydrochloride 896-71-9, Tigestol 909-14-8, Costatolide 909-39-7, Opipramol hydrochloride 911-45-5D, **Clomifene**, analogs 914-00-1, Methacycline 955-48-6, Metalol hydrochloride 956-90-1, Phencyclidine hydrochloride 959-10-4, Xenbucin 962-02-7, Nitrodan 963-39-3, Demoxepam 965-90-2, Ethylestrenol 967-48-6, Flubanilate hydrochloride 968-93-4, Testolactone 969-33-5, Cyproheptadine hydrochloride 972-02-1, Diphenidol 976-71-6, Canrenone 977-79-7, Medrogestone 980-71-2, Brompheniramine maleate 982-24-1, Clopenthixol 983-85-7, Penamecillin 985-16-0, Nafcillin sodium 987-02-0, Demecycline 987-78-0, Citicoline 990-73-8, Fentanyl citrate 1018-71-9, Pyrrolnitrin 1021-11-0, Guanoxyfen sulfate 1038-59-1, Glyoctamide 1050-48-2, Benzilonium bromide 1069-66-5, Valproate sodium 1070-11-7, Ethambutol hydrochloride 1070-95-7, Guanoctine hydrochloride 1094-08-2, Ethopropazine hydrochloride 1095-90-5, Methadone hydrochloride 1098-60-8, Triflupromazine hydrochloride 1104-22-9, Meclizine hydrochloride 1110-40-3, Cortivazol 1113-10-6, Guancydine 1115-70-4, Metformin hydrochloride 1134-47-0, Baclofen 1143-38-0, Anthralin 1146-98-1, Bromindione 1147-62-2, Pyrovalerone hydrochloride 1150-20-5, Azabon 1151-11-7, Ipodate calcium 1155-03-9, Zolamine hydrochloride 1156-19-0, Tolazamide 1172-18-5, Flurazepam hydrochloride 1173-88-2, Oxacillin sodium 1197-18-8, Cyclocapron 1197-21-3, Phentermine hydrochloride 1199-18-4, Oxidopamine 1211-28-5, Prolintane hydrochloride 1212-72-2, Mephentermine sulfate 1212-83-5, Guanisoquin sulfate 1218-35-5, Xylometazoline hydrochloride 1220-83-3, Sulfamonomethoxine 1225-20-3, Iothalamate sodium 1225-55-4, Protriptyline hydrochloride 1227-61-8, Mefexamide 1231-93-2, Ethynodiol 1232-85-5, Elantrine 1234-71-5, Namoxyrate 1235-15-0, Norbolethone 1242-56-4, Stenbolone acetate 1244-76-4 1252-69-3, Piperamide maleate 1253-28-7, Gestonorone caproate 1263-89-4, Paromomycin sulfate 1264-72-8, Colistin sulfate 1271-19-8, Titanocene dichloride 1314-95-0, Stannous sulfide 1319-82-0, Aminocaproic acid

1321-23-9, Chloroxylenol 1322-14-1, Calcium undecylenate 1323-83-7, Glycerol distearate 1336-78-3, Imidecyl iodine 1392-21-8, Kitasamycin 1397-89-3, Amphotericin B 1400-61-9, Nystatin 1402-82-0, Amphomycin 1403-17-4, Candicidin 1403-71-0, Hamycin 1403-99-2, Mitogillin 1404-00-8, Mitomycin 1404-08-6, Neutramycin 1404-15-5, Nogalamycin 1404-20-2, Peliomycin 1404-48-4, Relomycin 1404-59-7, Rutamycin 1404-64-4, Sparsomycin 1404-88-2, Tyrothricin 1404-90-6, Vancomycin 1404-93-9 1405-00-1, Viridofulvin 1405-20-5, Polymyxinbsulfate 1405-37-4, Capreomycin sulfate 1405-41-0, Gentamicin sulfate 1405-52-3, Sulfomyxin 1405-87-4, Bacitracin 1405-97-6, Gramicidin 1414-45-5, Nisin 1420-03-7, Propenzolate hydrochloride 1420-55-9, Thiethylperazine 1421-14-3, Propanidid 1424-00-6, Mesterolone 1432-75-3, Nitralamine hydrochloride 1456-52-6, Ioprocemic acid 1476-53-5, Novobiocin sodium 1477-40-3, Levomethadyl acetate 1491-81-2, Bolmantalate 1508-65-2, Oxybutynin chloride 1508-75-4, Tropicamide 1508-76-5, Procyclidine hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release active ingredients)

IT 1524-88-5, Flurandrenolide 1538-09-6 1553-34-0, Methixene hydrochloride 1553-60-2, Ibufenac 1597-82-6, Paramethasone acetate 1605-68-1, Taxane 1605-89-6, Bolasterone 1607-17-6, Pentrinitrol 1622-61-3, Clonazepam 1622-62-4, Flunitrazepam 1639-60-7, Propoxyphene hydrochloride 1642-54-2, Diethylcarbamazine citrate 1649-18-9, Azaperone 1661-29-6, Meturedepa 1665-48-1, Metaxalone 1684-40-8, Tacrine hydrochloride 1707-14-8, Phenmetrazine hydrochloride 1722-62-9, Mepivacaine hydrochloride 1740-22-3, Pyrinoline 1744-22-5, Riluzole 1764-85-8, Epithiazide 1786-81-8, Prilocaine hydrochloride 1808-12-4, Bromodiphenhydramine hydrochloride 1812-30-2, Bromazepam 1841-19-6, Fluspirilene 1847-63-8, Nafoxidine hydrochloride 1866-43-9, Rolodine 1867-66-9, Ketamine hydrochloride 1892-80-4, Fenethylline hydrochloride 1893-33-0, Pipamperone 1910-68-5, Methisazone 1977-10-2, Loxapine 1977-11-3, Perlapine 1980-45-6, Benzodepa 1982-37-2, Methdilazine 1986-53-4, Bolandiol dipropionate 2013-58-3, Meclocycline 2022-85-7, Flucytosine 2030-63-9, Clofazimine 2056-56-6, Cintazone 2058-52-8, Clothiapine 2062-78-4, Pimozide 2062-84-2, Benperidol 2068-78-2, Vincristine sulfate 2078-54-8, Propofol 2098-66-0, Cyproterone 2109-73-1, Butacetin 2119-75-7, Fluperolone acetate 2127-01-7, Clorexolone 2135-14-0, Descinolone acetonide 2135-17-3, Flumethasone 2152-34-3, Pemoline 2154-02-1, Methopholine 2167-85-3, Pipazethate 2169-64-4, Azaribine 2181-04-6, Canrenoate potassium 2210-77-7, Pyrrocaine 2218-68-0, Chloral betaine 2244-21-5, Troclosene potassium 2259-96-3, Cyclothiazide 2276-90-6, Iothalamic acid 2313-87-3, Ethoxazene hydrochloride 2315-02-8, Oxymetazoline hydrochloride 2321-07-5, Fluorescein 2324-94-9, Profadol hydrochloride 2353-33-5, Decitabine 2364-72-9, Cyprolidol hydrochloride 2391-03-9, Dexbrompheniramine maleate 2398-96-1, Tolnaftate 2438-32-6, Dexchlorpheniramine maleate 2441-88-5, Fenyripol hydrochloride 2447-57-6, Sulfadoxine 2465-59-0, Oxypurinol 2487-63-0, Quinbolone 2508-79-4, Methyldopate hydrochloride 2521-01-9, Encyprate 2529-45-5, Flurogestone acetate 2607-06-9, Diflucortolone 2608-24-4, Piposulfan 2612-33-1, Clonitrate 2618-25-9, Ioglycamic acid 2668-66-8, Medrysone 2687-96-9 2740-04-7, Dimefline hydrochloride 2750-76-7, Rifamide 2751-09-9, Troleandomycin 2753-45-9, Mebeverine hydrochloride 2768-90-3, Quinaldine blue 2809-21-4, Etidronic acid 2825-60-7, Formocortal 2829-19-8, Rolicyprine 2856-75-9, Modaline sulfate 2898-11-5, Medazepam hydrochloride 2898-13-7, Sulazepam 2919-66-6, Melengestrol acetate 2921-92-8, Propatyl nitrate 2955-38-6, Prazepam 2975-34-0, Carphenazine maleate 2988-32-1, Indriline hydrochloride 2998-57-4, Estramustine 3000-39-3, Quingestanol acetate 3044-32-4, Clogestone acetate 3056-17-5, Stavudine 3073-59-4, Hexamethylene bisacetamide 3093-35-4, Halcinonide 3105-97-3, Hycanthone 3115-05-7, Iobenzamic acid 3116-76-5, Dicloxacillin 3122-01-8, Thiazesim hydrochloride 3124-93-4, Ethynerone 3137-73-3, Anagestone acetate 3200-06-4, Nafronyl oxalate 3202-55-9, Benapryzine hydrochloride 3211-76-5, Selenomethionine 3239-45-0, Dexfenfluramine hydrochloride 3270-71-1, Nifuraldezone 3282-75-5, Ethanolamine oleate 3313-26-6, Thiothixene 3374-05-8, Nalidixate sodium 3385-03-3, Flunisolide 3416-26-0, Lidoflazine 3440-28-6, Betamipron 3459-20-9,

Glymidine sodium 3485-14-1, Cyclacillin 3485-62-9, Clidinium bromide 3505-38-2, Carbinoxamine maleate 3511-16-8, Hetacillin 3521-84-4, Iodipamide meglumine 3538-57-6, Haloprogesterone 3546-41-6, Pyrvinium pamoate 3562-84-3, Benzbromarone 3570-10-3, Benorterone 3570-75-0, Nifurthiazole 3572-80-3, Cyclazocine 3577-01-3, Cephaloglycin 3599-32-4, Indocyanine green 3601-19-2, Ropizine 3614-69-5, Dimethindene maleate 3624-96-2, Bialamicol hydrochloride 3666-69-1, Dioxadrol hydrochloride 3688-85-5, Diapamide 3693-39-8, Flucloronide 3696-28-4, Dipyrithione 3704-09-4, Mibolerone 3715-90-0, Tramazoline hydrochloride 3717-88-2, Flavoxate hydrochloride 3734-16-5, Prodilidine hydrochloride 3735-90-8, Phencarbamide 3737-09-5, Disopyramide 3771-19-5, Nafenopin 3778-73-2, Ifosfamide 3784-99-4, Stilbazium iodide 3791-63-7 3795-88-8, Levofuraltadone 3810-74-0, Streptomycin sulfate 3810-80-8, Diphenoxylate hydrochloride 3819-00-9, Piperacetazine 3845-22-5, Teroxalene hydrochloride 3858-89-7, Chloroprocaine hydrochloride 3861-73-2, Anazolene sodium 3876-10-6, Clominorex 3930-19-6, Streptonigrin 3930-20-9, Sotalol 3978-86-7, Azatadine maleate 4015-32-1, Quazodine 4105-38-8 4117-65-1, Aspartocin 4171-13-5, Valnoctamide 4197-24-4, Carbol-Fuchsin 4205-90-7, Clonidine 4258-85-9, Clocortolone acetate 4268-36-4, Tybamate 4291-63-8, Cladribine 4320-13-2, Thiazinamium chloride 4330-99-8, Trimeprazine tartrate 4342-03-4, Dacarbazine 4386-35-0, Meralein sodium 4434-20-2, Clothixamide maleate 4499-40-5, Oxtriphylline 4548-15-6, Flunidazole 4551-59-1, Fenalamide 4598-67-8 4663-83-6, Buramate 4682-36-4, Orphenadrine citrate 4724-59-8, Clamoxyquin hydrochloride 4759-48-2, Isotretinoin 4803-27-4, Anthramycin 4803-44-5, Levopropylcillin potassium 4803-45-6, Thiphencillin potassium 4936-47-4, Nifuratel 4991-68-8, Pimetine hydrochloride 5002-47-1, Fluphenazine decanoate 5034-76-4, Indoxole 5036-03-3, Nifurdazil 5051-62-7, Guanabenz 5053-06-5, Fenspiride 5055-20-9, Nifurquinazol 5055-42-5, Silandrone 5072-26-4, Buthionine sulfoximine 5086-74-8, Tetramisole hydrochloride 5090-37-9, Metizoline hydrochloride 5104-49-4, Flurbiprofen 5118-17-2, Furazolium chloride 5250-39-5, Floxacillin 5251-34-3, Cloprednol 5289-74-7, Ecdysterone 5318-76-3, Imidocarb hydrochloride 5322-53-2, Oxiperomide 5355-16-8, Diaveridine 5370-01-4, Mexiletine hydrochloride 5373-42-2, Thaliblastine 5467-78-7, Fenamole 5490-27-7, Dihydrostreptomycin sulfate 5508-58-7, Andrographolide 5522-33-8, Difluanine hydrochloride 5534-09-8, Beclomethasone dipropionate 5536-17-4, Vidarabine 5560-62-3, Biphenamine hydrochloride 5560-69-0, Ethyl dibunate 5560-72-5, Iprindole 5560-73-6, Mimbane hydrochloride 5560-75-8, Pyroxamine maleate 5560-77-0, Rotoxamine 5560-78-1, Teclozan 5578-73-4, Sanguinarium chloride 5579-13-5, Capuride 5579-16-8, Epinephryl borate 5579-27-1, Simtrazene 5579-85-1, Bromchlorenone 5579-92-0, Iopydol 5579-93-1, Iopydone 5579-94-2, merisoprol Hg 197 5579-95-3, Nifurmerone 5581-35-1, Amphecloral 5581-40-8, Dimefadane 5581-42-0, Glyparamide 5581-46-4, Molinazone
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release active ingredients)

IT 5581-52-2, Thiamiprine 5585-59-1, Nitrocycline 5585-60-4, Paranyline hydrochloride 5585-62-6 5585-71-7, Benzindopyrine hydrochloride 5585-73-9, Butriptyline hydrochloride 5586-87-8, Mefenorex hydrochloride 5588-20-5, Chlordantoin 5588-21-6, Cintriamide 5588-23-8, Cypenamine hydrochloride 5588-25-0, Dihexyverine hydrochloride 5588-29-4, Fenmetramide 5588-31-8, Imidoline hydrochloride 5588-33-0, Mesoridazine 5588-38-5, Tolpyrramide 5591-22-0, Becanthone hydrochloride 5591-27-5, Clometherone 5591-29-7, Etafedrine hydrochloride 5591-33-3, Iosefamic acid 5591-43-5, Solypertine tartrate 5591-44-6, Pyrroliphene hydrochloride 5611-64-3, Methalthiazide 5630-53-5, Tibolone 5633-14-7, Benzetimide hydrochloride 5633-25-0, Noracymethadol hydrochloride 5634-37-7, Clorethate 5634-38-8, Guaithylline 5634-40-2, Levamfetamine succinate 5634-41-3, Parapenzolate bromide 5634-42-4, Tocamphyl 5667-70-9, Pentabamate 5667-71-0, Streptonicozid 5696-06-0, Methetoin 5696-09-3, Proxazole 5696-15-1, Butoxamine hydrochloride 5696-17-3, Epipropidine 5714-04-5, Guanoxan sulfate 5714-05-6, Quindecamine acetate 5714-75-0, Prednazate 5714-76-1, Quinetolate 5714-82-9, Triclofenol piperazine 5714-90-9, Levopropoxyphene napsylate

5716-20-1, Bamethan sulfate 5728-52-9, Felbinac 5749-67-7, Carbaspirin calcium 5781-37-3, Cycliramine maleate 5786-21-0, Clozapine 5786-68-5, Quipazine maleate 5800-19-1, Metiapine 5863-35-4, Nitromifene citrate 5870-29-1, Cyclopentolate hydrochloride 5875-06-9, Proparacaine hydrochloride 5928-84-7, Penicillinvbenzathine 5964-24-9, Thimerfonate sodium 5965-13-9, Dihydrocodeine bitartrate 5977-10-6, Fencibutirol 5980-31-4, Hexedine 5987-82-6, Benoxinate hydrochloride 6054-98-4, Olsalazine sodium 6157-87-5, Trestolone acetate 6190-39-2, Dihydroergotamine mesylate 6284-40-8, Meglumine 6385-02-0, Meclofenamate sodium 6385-58-6, Bithionolate sodium 6443-40-9, Xylamidine tosylate 6452-73-9, Oxprenolol hydrochloride 6493-05-6, Pentoxifylline 6500-81-8, Ethacrynate sodium 6533-00-2, Norgestrel 6556-11-2, Inositol niacinate 6576-51-8, Stallimycin hydrochloride 6591-72-6, Penicillinvhydrabamine 6620-60-6, Proglumide 6639-99-2, 17-α-Dihydroequilenin 6673-35-4, Practolol 6673-97-8, Spiroxasone 6724-53-4, Perhexiline maleate 6804-07-5, Carbadox 6830-17-7, Oxamarin hydrochloride 6890-40-0, Histamine phosphate 6933-90-0, Clorprenaline hydrochloride 6981-18-6, Ormetoprim 6990-06-3, Fusidic acid 7004-98-0, Epimestrol 7013-41-4, Talopram hydrochloride 7019-69-4 7054-25-3, Quinidine gluconate 7082-27-1, Trimoxamine hydrochloride 7082-29-3, Ampyzine sulfate 7082-30-6, Triampyzine sulfate 7125-67-9, Metoquizine 7125-70-4, Amiquinsin hydrochloride 7125-71-5, Toquizine 7125-73-7, Flumetramide 7125-76-0, Codoxime 7195-27-9, Mefruside 7199-29-3, Cyheptamide 7225-61-8, Metrizoate sodium 7232-51-1, Pararosaniline pamoate 7241-94-3, Zolertine hydrochloride 7246-20-0, Triclofos sodium 7246-21-1, Tyropanoate sodium 7247-57-6, Heteronium bromide 7261-97-4, Dantrolene 7262-00-2, Quinazosin hydrochloride 7273-99-6, Gamfexine 7280-37-7, Estropipate 7281-31-4, Vinglycinate sulfate 7297-25-8, Erythrityl tetranitrate 7414-83-7, Etidronate disodium 7421-40-1, Carbenoxolone sodium 7424-00-2, Fenclonine 7439-94-3, Lutetium 7439-97-6, Mercury 7440-06-4D, Platinum, compds. 7440-57-5, Gold 7447-40-7, Potassium chloride 7481-89-2, Zalcitabine 7487-88-9, Magnesium sulfate 7491-74-9, Piracetam 7492-29-7, Clazolam 7553-56-2, Iodine 7554-65-6, Fomepizole 7601-55-0, Metocurine iodide 7644-67-9, Azotomycin 7660-71-1, Mesuprine hydrochloride 7681-11-0, Potassium iodide 7681-54-1, Indomethacin sodium 7681-76-7, Ronidazole 7681-80-3, Pentapiperium methylsulfate 7681-93-8, Natamycin 7689-03-4D, Camptothecin, derivs. 7698-97-7, Fenestrel 7720-78-7, Ferrous sulfate 7722-64-7, Potassium permanganate 7722-84-1, :Hydrogen peroxide 7724-76-7, Riboprine 7761-45-7, Metoprine 7761-88-8, Silver nitrate 8008-53-5, Ethiodized Oil 8017-57-0, Trisulfapyrimidine 8025-81-8, Spiramycin 8029-68-3, Ichthammol 8029-99-0, Paregoric 8031-09-2, Sodium morrhuate 8031-14-9, Oxychlorosene 8052-16-2, Cactinomycin 8063-91-0, Mirincamycin hydrochloride 8065-29-0, Liotrix 8067-24-1, Ergoloid mesylates 8067-69-4, Halquinols 8068-28-8, Colistimethate sodium 9000-99-1, Brinolase 9002-04-4, Thrombin 9002-60-2, Corticotropin 9002-61-3, Human chorionic gonadotropin 9002-67-9, Luteinizing hormone 9002-69-1, Relaxin 9003-20-7, Polyvinyl acetate 9003-21-8, Poly (methyl acrylate) 9003-42-3, Poly(ethyl methacrylate) 9003-63-8, Poly(butyl methacrylate) 9004-10-8, Insulin 9004-35-7 9004-36-8, Cellulose acetate butyrate 9004-38-0, Cellulose acetate phthalate 9004-39-1, Cellulose acetate propionate 9004-48-2, Cellulose propionate 9004-57-3, Ethylcellulose 9007-12-9, Calcitonin 9007-92-5, Glucagon 9008-05-3, Histoplasmin 9010-01-9, Sodium amylosulfate 9010-88-2, eudragit NE30D 9011-14-7, Poly(methyl methacrylate) 9011-15-8, Poly(isobutyl methacrylate) 9011-93-2, Lysostaphin 9012-09-3 9012-76-4, Poliglusam 9014-02-2, Zinostatin 9014-42-0, Thrombopoietin 9015-68-3, Asparaginase 9039-53-6, Urokinase 9041-08-1, Ardeparin sodium 9041-93-4, Bleomycin sulfate 9046-56-4, Ancrod 9050-67-3, Sizofiran 9051-97-2D, 1,3-β-Glucan, carboxymethylated 9054-89-1, Orgotein 9087-70-1, Aprotinin 10024-97-2, Nitrous oxide 10043-49-9, Au 198 10078-46-3, Roletamide 10085-81-1, Benzoctamine hydrochloride 10087-89-5, Enpromate 10118-85-1, Lydimycin 10118-90-8, Minocycline 10238-21-8, Glyburide 10262-69-8, Maprotiline 10310-32-4, Tribenoside 10318-26-0, Mitolactol 10322-73-3, Estrofurate 10351-50-5, Leniquinsin 10355-14-3, Boxidine 10389-72-7, Clortermine hydrochloride 10397-75-8, Iocarmic acid 10403-51-7, Mitindomide 10418-03-8, Stanozolol 10423-37-7, Citenamide

10457-90-6, Bromperidol 10488-36-5 10540-29-1, Tamoxifen 10540-97-3, Memotine hydrochloride 10549-91-4, Meclorisone dibutyrate 10563-70-9, Melitracen hydrochloride 10596-23-3, Clodronic acid 11000-17-2, Vasopressin 11002-22-5, Apurinic acid 11006-76-1, Virginiamycin 11006-77-2, Statolon 11015-37-5, Bambermycin 11016-07-2, Fungimycin 11028-00-5, Bacoside A 11029-06-4, Elemene 11033-34-4, Steffimycin 11041-12-6, Cholestyramine resin 11043-98-4, Mitocromin 11043-99-5, Mitomalcin 11048-13-8, Nebramycin 11048-15-0, Kalafungin 11048-52-5 11051-71-1, Avilamycin 11056-09-0, Ranimycin 11056-11-4, Biniramycin 11056-12-5, Cirolemycin 11056-13-6, Denofungin 11056-14-7, Mitocarcin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release active ingredients)

IT 11056-15-8, Mitosper 11056-18-1, Scopafungin 11056-20-5, Zorbamycin 11078-21-0, Filipin 11096-49-4, Partricin 11121-32-7, Mepartricin 12192-57-3, Aurothioglucose 12622-73-0, Coccidioidin 12629-01-5, Somatropin 12706-94-4, Anthelmycin 12713-07-4D, Verdin, derivs. 13010-47-4, Lomustine 13055-82-8, Reproterol hydrochloride 13060-14-5, Yangambin 13071-11-9, Dexpropranolol hydrochloride 13103-34-9, Boldenone undecylenate 13115-40-7, Fonazine mesylate 13292-46-1, Rifampin 13379-87-8, Tiprenolol hydrochloride 13392-18-2, Fenoterol 13392-28-4, Rimantadine 13408-29-2, Nitroxide 13411-16-0, Nifurpirinol 13422-16-7, Triflocin 13463-41-7, Pyrithione zinc 13494-90-1, Gallium nitrate 13523-86-9, Pindolol 13539-59-8, Apazone 13551-87-6, Misonidazole 13647-35-3, Trilostane 13665-88-8, Mopidamol 13698-49-2, Delmadinone acetate 13758-23-1, Quinterenol sulfate 13838-16-9, Enflurane 13909-09-6, Semustine 13958-40-2, Oxiramide 14008-44-7, Metopimazine 14008-46-9, Pinoxepin hydrochloride 14028-44-5, Amoxapine 14088-71-2, Proclonol 14176-10-4, Cetiedil 14176-50-2, Tiletamine hydrochloride 14188-82-0, Cytostatin 14255-87-9, Parbendazole 14265-71-5, selenium 75 14293-44-8, Xipamide 14402-89-2, Sodium nitroprusside 14437-41-3, Clioxanide 14484-47-0, Deflazacort 14561-42-3, Menoctone 14611-51-9, Selegiline 14611-52-0, Selegiline hydrochloride 14636-12-5, Terlipressin 14698-29-4, Oxolinic acid 14769-73-4, Levamisole 14769-74-5, Dexamisole 14796-24-8, Cinperene 14796-28-2, Clodanolene 14816-67-2, Soterenol hydrochloride 14885-29-1, Ipronidazole 14930-96-2, Cytochalasin B 15037-55-5, Ethonam nitrate 15176-29-1, Edoxudine 15179-97-2, Estrazinol hydrobromide 15180-00-4, Prednival 15221-81-5, Fludorex 15256-58-3, Beloxamide 15307-79-6, Diclofenac sodium 15318-45-3, Thiamphenicol 15468-10-7, Oxidronic acid 15478-78-1, Iodamide 15500-66-0, Pancuronium bromide 15574-96-6, Pizotyline 15578-26-4, Stannous pyrophosphate 15622-65-8, Molindone hydrochloride 15639-50-6, Safingol 15663-27-1, Cisplatin 15676-16-1, Sulpiride 15686-51-8, Clemastine 15686-68-7, Volazocine 15686-71-2, Cephalexin 15686-74-5, Cyclophenazine hydrochloride 15686-91-6, Propiram 15687-07-7, Cyprazepam 15687-27-1, Ibuprofen 15722-48-2, Olsalazine 15793-40-5, Terodiline 15826-37-6, Cromolyn sodium 15922-78-8, Pyrithione sodium 15992-13-9, Intrazole 16034-77-8, Iocetamic acid 16051-77-7, Isosorbide mononitrate 16231-75-7, Atolide 16320-04-0, Gestrinone 16590-41-3, Naltrexone 16624-40-1 16662-47-8, Gallopamil 16676-27-0, Nalmexone hydrochloride 16679-58-6, Desmopressin 16773-42-5, Ornidazole 16816-67-4, Pantethine 16846-24-5, Josamycin 16915-71-2, Cingestol 16915-78-9, Bolenol 16915-79-0, Mequidox 16915-80-3, Oxogestone phenpropionate 16960-16-0, Cosyntropin 17021-26-0, Calusterone 17033-82-8, iomethini125 17090-79-8, Monensin 17196-88-2, Vincofos 17230-85-2, Amquinate 17230-86-3, Carbenicillin potassium 17230-87-4, Seperidol hydrochloride 17230-88-5, Danazol 17230-89-6, Nimazone 17243-32-2, Ketipramine fumarate 17243-64-0, Piprozolin 17289-49-5, Tetrydamine 17321-77-6, Clomipramine hydrochloride 17560-51-9, Metolazone 17598-65-1, Deslanoside 17605-73-1, Colterol mesylate 17650-98-5, Ceruletide 17737-65-4, Clonixin 17784-12-2, Sulfacytine 17902-23-7, Tegafur 18010-40-7, Bupivacaine hydrochloride 18046-21-4, Fentiazac 18109-81-4, Butamirate citrate 18174-58-8, Pipoxolan hydrochloride 18323-44-9, Clindamycin 18378-89-7, Plicamycin 18416-85-8, Lombricine 18464-39-6, Caroxazone 18472-51-0, Chlorhexidine gluconate 18559-94-9, Salbutamol 18588-57-3, Etoprine 18641-57-1, Glyceryl behenate 18694-40-1, Epirizole 18883-66-4, Streptozocin 18917-89-0, Magnesium salicylate 18965-97-4,

Berlafenone 18984-80-0, Euprocin hydrochloride 19216-56-9, Prazosin 19237-84-4, Prazosin hydrochloride 19291-69-1, Gestaclone 19356-17-3, Calcifediol 19561-70-7, Nifuratrone 19825-63-9, Pirnabine 19863-06-0, Ioxotrizoic acid 19885-51-9, Aranotin 19888-56-3, Fluazacort 19916-73-5, O6-Benzylguanine 19992-80-4, Butixirate 20064-19-1, Propionylcarnitine 20098-14-0, Idramantone 20187-55-7, Bendazac 20287-37-0, Fenquizone 20350-15-6, Brefeldin 20423-99-8, Deprodone 20554-84-1, Parthenolide 20559-55-1, Oxibendazole 20638-84-0, Retinamide 20684-06-4, Bamifylline hydrochloride 20830-75-5, Digoxin 21059-48-3, Veramine 21132-59-2, Pazoxide 21221-18-1, Flazalone 21256-18-8, Oxaprozin 21365-49-1, Tralonide 21434-91-3, Capobenic acid 21440-97-1, Brofoxine 21498-08-8, Lofexidine hydrochloride 21535-47-7, Mianserin hydrochloride 21626-89-1, Diftalone 21638-36-8, Nifurimide 21736-83-4, Spectinomycin hydrochloride 21738-42-1, Oxamniquine 21791-39-9, Letimide hydrochloride 21820-82-6, Fenpipalone 21829-22-1, Clonixeril 21829-25-4, Nifedipine 21888-98-2, Dexetimide 21925-88-2, Tesicam 22012-72-2, Zilantel 22071-15-4, Ketoprofen 22161-81-5, Dexketoprofen 22195-34-2, Guanadrel sulfate 22199-46-8, Clomacran phosphate 22204-24-6, Pyrantel Pamoate 22204-53-1, Naproxen 22204-91-7, Lifibrate 22232-71-9, Mazindol 22254-24-6, Ipratropium bromide 22316-47-8, Clobazam 22365-40-8, Triflubazam 22461-13-8, Fantridone hydrochloride 22484-64-6, Sulfanilate zinc 22494-27-5, Flufenisal 22494-42-4, Diflunisal 22632-06-0, Bupicomide 22662-39-1, Rafoxanide 22664-55-7, Metipranolol 22668-01-5, Etanidazole 22737-01-5, Diflumidone sodium 22760-18-5, Proquazone 22916-38-7, Orconazole nitrate 22916-47-8, Miconazole 23031-32-5, Terbutaline sulfate 23076-35-9, Xylazine hydrochloride 23092-17-3, Halazepam 23155-02-4, Fosfomycin 23163-51-1, Methynodiol diacetate 23226-37-1, Daledalin tosylate 23239-36-3, Deterenol hydrochloride 23239-37-4, Etoxadrol hydrochloride 23239-41-0, Cephacetrile sodium 23239-78-3, Pridefine hydrochloride 23247-36-1, Nafomine malate 23256-09-9, Closiramine aceturate 23256-26-0, Piquizil hydrochloride 23256-28-2, Hoquizil hydrochloride 23256-50-0, Guanabenz acetate 23257-58-1, Levoxadrol hydrochloride 23277-43-2, Nalbuphine hydrochloride 23277-50-1, Salicylate meglumine 23288-49-5, Probucol 23313-80-6, Epitetracycline hydrochloride 23319-48-4, Megalomicin potassium phosphate 23327-57-3, Nefopam hydrochloride 23444-86-2, Suncillin sodium 23469-05-8, Diamocaine cyclamate 23478-02-6, 16-α-Gitoxin 23486-22-8, Esproquin hydrochloride 23541-50-6, Daunorubicin hydrochloride 23593-75-1, Clotrimazole
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release active ingredients)

IT 23607-71-8, Fetoxylate hydrochloride 23672-07-3, Levosulpiride 23674-86-4, Difluprednate 23712-05-2, Fenmetozole hydrochloride 23736-58-5, Cloxacillin benzathine 23757-42-8, Midaflur 23779-99-9, Floctafenine 23915-74-4, Trebenzomine hydrochloride 24047-25-4, Guanoxabenz 24233-80-5, Bisobrin lactate 24243-89-8, Triflumidate 24280-93-1, Mycophenolic acid 24305-27-9, Protirelin 24353-88-6, Lorbamate 24356-60-3, Cephapirin sodium 24357-98-0, Isomylamine hydrochloride 24358-76-7, Nivazol 24358-84-7, Dexivacaine 24359-14-6, liothyroninei125 24359-16-8 24360-55-2, Milipertine 24381-55-3, Salethamide maleate 24428-71-5, Glicetanile sodium 24584-09-6, Dexrazoxane 24678-13-5, Lenperone 24967-94-0, Dermatan sulfate 25053-27-4, Lyapolate sodium 25087-17-6, Poly (hexyl methacrylate) 25092-41-5, Norgestomet 25122-46-7, Clobetasol propionate 25122-57-0, Clobetasone butyrate 25126-32-3, Sincalide 25127-31-5, Cidoxepin hydrochloride 25155-18-4, Methylbenzethonium chloride 25189-01-9, Poly(phenyl methacrylate) 25269-04-9, Nisobamate 25314-87-8, Elucaine 25332-39-2, Trazodone hydrochloride 25387-70-6, Dazadrol maleate 25389-94-0, Kanamycin sulfate 25451-15-4, Felbamate 25496-72-4, Glycerol monooleate 25614-03-3, Bromocriptine 25655-41-8, Povidone-Iodine 25717-80-0, Molsidomine 25719-52-2, Poly (lauryl methacrylate) 25775-90-0, Zucapsaicin 25812-30-0, Gemfibrozil 25827-13-8, Suloxifen oxalate 25905-77-5, Minaprine 25953-19-9, Cefazolin 25986-77-0, Poly (octadecyl acrylate) 26048-05-5, Beauvericin 26097-80-3, Cambendazole 26124-32-3, Poly (isopropyl acrylate) 26155-31-7, Morantel tartrate 26159-36-4, Naproxol

26171-23-3, Tolmetin 26304-61-0, Azepindole 26308-28-1, Ripazepam 26309-95-5, Pivampicillin hydrochloride 26335-74-0, Poly (isobutyl acrylate) 26538-44-3, Zeranol 26615-21-4, Zotepine 26652-09-5, Ritodrine 26675-46-7, Isoflurane 26718-25-2, Halofenate 26774-90-3, Epicillin 26786-32-3, Lofepramine hydrochloride 26786-84-5, Lomofungin 26787-78-0, Amoxicillin 26807-65-8, Indapamide 26839-75-8, Timolol 26844-12-2, Indoramin 26849-57-0, Triclonide 26864-56-2, Penfluridol 26944-48-9, Glibornuride 27107-79-5, Tilidine hydrochloride 27220-47-9, Econazole 27223-35-4, Ketazolam 27262-47-1, Levobupivacaine 27276-25-1, Capobenate sodium 27302-90-5, Oxisuran 27314-97-2, Tirapazamine 27466-29-1, Intriptyline hydrochloride 27511-99-5, Eterobarb 27523-40-6, Isoconazole 27548-93-2, baccatin III 27589-33-9, Azosemide 27591-69-1, Tilorone hydrochloride 27686-84-6, Masoprocol 27724-96-5, Cetraxate hydrochloride 27737-38-8, Mixidine 27762-78-3, Kethoxal 27823-62-7, Chlortetracycline bisulfate 27848-84-6, Nicergoline 27877-51-6, Tolindate 28069-65-0, Cuprimyxin 28395-03-1 28523-86-6, Sevoflurane 28546-58-9, Uldazepam 28657-80-9, Cinoxacin 28721-07-5, Oxcarbazepine 28745-68-8, Thiofedrine 28782-42-5, Difenoxin 28841-62-5, Atrinositol 28860-95-9, Carbidopa 28911-01-5, Triazolam 29050-11-1, Seclazone 29053-27-8, Meseclazone 29069-24-7, Prednimustine 29094-61-9, Glipizide 29110-48-3, Guanfacine hydrochloride 29121-60-6, Vaninolol 29122-68-7, Atenolol 29334-07-4, Sulmarin 29342-05-0, Ciclopirox 29462-18-8, Bentazepam 29679-58-1, Fenoprofen 29767-20-2, Teniposide 29868-97-1, Pirenzepine hydrochloride 29975-16-4, Estazolam 30060-91-4, Lometraline hydrochloride 30236-32-9, Dexsotalol 30303-65-2, Docosanol 30387-51-0, Asperlin 30392-41-7, Bitolterol mesylate 30516-87-1, Zidovudine 30544-47-9, Etofenamate 30652-11-0, Deferiprone 30716-01-9, Emilium tosylate 30868-30-5, Pyrazofurin 30910-27-1, Treloxinate 31112-62-6, Metrizamide 31127-82-9, Iodoxamide 31428-61-2, Tiamenidine 31430-15-6, Flubendazole 31430-18-9, Nocodazole 31431-39-7, Mebendazole 31431-43-3, Cyclobendazole 31441-78-8, Mercaptopurine 31478-45-2, Bamnidazole 31677-93-7, Bupropion hydrochloride 31793-07-4, Pirprofen 31842-01-0, Indoprofen 31842-61-2, Rimiterol hydrobromide 31855-75-1 31883-05-3, Moracizine 31932-09-9, Ticarbodine 31959-88-3, Clodazon hydrochloride 31969-05-8, Bunolol hydrochloride 32211-97-5, Cyclindole 32222-06-3, Calcitriol 32266-10-7, Hexoprenaline sulfate 32295-18-4, Tosifen 32385-11-8, Sisomicin 32462-30-9, Oxfenicine 32780-64-6, Labetalol hydrochloride 32795-47-4, Nomifensine maleate 32954-58-8, Ipomeanol 32986-56-4, Tobramycin 33025-33-1 33069-62-4, Paclitaxel 33089-61-1, Amitraz 33125-97-2, Etomidate 33144-79-5, Broperamole 33159-27-2, Ecabet 33237-74-0, Aprindine hydrochloride 33286-22-5, Diltiazem hydrochloride 33386-08-2, Buspirone hydrochloride 33402-03-8, Metaraminol bitartrate 33419-42-0, Etoposide 33434-24-1, eudragit RL 33515-09-2, Gonadorelin 33564-31-7, Diflorasone diacetate 33754-49-3, Zolazepam hydrochloride 33765-68-3, Oxendolone 33774-52-6, Detajmium bitartrate 33813-84-2, Deprostil 33876-97-0, Linsidomine 34031-32-8, Auranofin 34042-85-8, Sudoxicam 34061-34-2 34114-01-7, Pemerid nitrate 34144-82-6 34157-83-0, Celastrol 34183-22-7, Propafenone hydrochloride 34214-49-8, Phenbutazone sodium glycerate 34256-91-2, Naranol hydrochloride 34297-34-2, Anidoxime 34368-04-2, Dobutamine 34444-01-4, Cefamandole 34482-99-0, Fletazepam 34522-46-8, Oxetorone fumarate 34552-83-5, Loperamide hydrochloride 34552-84-6, Isoxicam 34580-14-8, Ketotifen fumarate 34645-84-6, Fenclofenac 34661-75-1, Urapidil 34839-70-8, Metiamide 34866-46-1, Carbuterol hydrochloride 34887-52-0, Fenisorex 34966-41-1, Cartazolate 35100-44-8, Endrysone 35115-60-7, Teprotide 35121-78-9, Epoprostenol 35135-67-2, Cormethasone acetate 35189-28-7, Norgestimate 35212-22-7, Ipriflavone 35273-88-2, Gliflumide 35301-24-7, Cedefingol 35322-07-7, Fosazepam 35423-09-7, Tesimide 35425-83-3, Quinuclium bromide 35449-36-6, Gemcadiol 35523-45-6, Fludalanine 35554-44-0, Enilconazole 35578-20-2, Oxarbazole 35604-67-2, Viloxazine hydrochloride 35607-20-6, Avridine 35607-66-0, Cefoxitin 35700-23-3, Carboprost 35764-29-5, Fluotracen hydrochloride 35795-17-6, Trimazosin hydrochloride 35834-26-5, Rosaramicin 35838-58-5, Etazolate hydrochloride 35846-53-8, Maitansine 35941-71-0, Tiaramide hydrochloride 35943-35-2, Triciribine 36167-63-2, Halofantrine hydrochloride 36282-47-0, Tramadol hydrochloride 36292-69-0,

Ketazocine 36322-90-4, Piroxicam 36330-85-5, Fenbufen 36504-94-6, Butaclamol hydrochloride 36505-82-5, Prodolic acid 36508-71-1, Zorubicin hydrochloride
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release active ingredients)

IT 36616-52-1, Fenclorac 36637-18-0, Etidocaine 36653-82-4, Cetyl alcohol 36735-22-5, Quazepam 36740-73-5, Flumizole 36791-04-5, Ribavirin 36945-03-6, Lergotrile 36950-96-6, Cicloprofen 36981-91-6, Fepradinol 36983-81-0, Fosfonet sodium 37025-55-1, Carbetocin 37087-94-8, Tibric acid 37091-66-0, Azlocillin 37106-97-1, Bentiromide 37200-12-7, Poly(isodecyl methacrylate) 37270-89-6, Nadroparin calcium 37296-80-3 37321-09-8, Apramycin 37332-99-3, Avoparcin 37517-26-3, Pipotiazine palmitate 37554-40-8, Fluquazone 37640-71-4, Aprindine 37661-08-8, Bacampicillin hydrochloride 37686-84-3, Terguride 37717-21-8, Flurocitabine 37723-78-7, Iopronic acid 37750-83-7, Rimoprogin 37751-39-6, Ciclazindol 37800-79-6 37863-70-0, Iosumetic acid 38070-41-6, Tiodonium chloride 38081-67-3, Carmantadine 38103-61-6, Tolamolol 38194-50-2, Sulindac 38241-28-0, Zinterol hydrochloride 38241-39-3, Tazolol hydrochloride 38270-90-5, strontium chloride Sr 89 38274-54-3, Benurestat 38304-91-5, Minoxidil 38321-02-7, Dexverapamil 38363-32-5, Penbutolol sulfate 38677-85-9, Flunixin 38821-53-3, Cephradine 38821-80-6, Rodocaine 38873-55-1, Furobufen 38955-22-5, Pinadoline 39022-39-4, Oxaprotiline hydrochloride 39186-49-7, Pirolazamide 39236-46-9, Imidurea 39294-79-6, Seractide acetate 39324-30-6, Pepstatin 39325-01-4, Picibanil 39562-70-4, Nitrendipine 39624-65-2, Azanator maleate 39624-66-3, Trepipam maleate 39698-78-7, Saralasin acetate 39791-20-3, Nylestriol 39809-25-1, Penciclovir 39878-70-1, Talampicillin hydrochloride 40034-42-2, Rosoxacin 40054-69-1, Etizolam 40180-04-9, Ticrynafen 40391-99-9, Pamidronic acid 40507-23-1, Fluproquazone 40594-09-0, Flucindole 40691-50-7, Tixanox 40759-33-9, Nolinium bromide 40796-97-2, Bemesetron 40819-93-0, Lorajmine hydrochloride 40828-44-2, Clazolimine 40828-45-3, Azolimine 40828-46-4, Suprofen 40966-79-8, Sarpicillin 41020-67-1, Mexrenoate potassium 41020-79-5, Dicirenone 41078-02-8, Enprofylline 41094-88-6, Tracazolate 41113-86-4, Bromoxanide 41147-04-0, Xanoxate sodium 41340-25-4, Etodolac 41570-61-0, Tulobuterol 41575-94-4, Carboplatin 41692-24-4 41708-72-9, Tocainide 41729-52-6, Dezaguanine 41767-29-7, Fluocortin butyl 41859-67-0, Bezafibrate 41927-88-2, sodium iodide 123 41964-07-2, Tolimidone 41992-22-7, Spirogermanium hydrochloride 42021-34-1, Biriperone 42045-97-6, Phenaridine 42116-76-7, Carnidazole 42116-77-8 42200-33-9, Nadolol 42220-21-3, iodocholesteroli131 42281-59-4, Oxilorphan 42408-78-6, Pirandamine hydrochloride 42408-82-2, Butorphanol 42422-68-4, Taleranol 42461-78-9, Sulfonterol hydrochloride 42616-25-1, Methioninase 42779-82-8, Clopirac 42794-76-3, Midodrine 42835-25-6, Flumequine 42864-78-8, Bevantolol hydrochloride 42877-18-9, Pelanserin hydrochloride 42879-47-0, Pranolium chloride 42924-53-8, Nabumetone 42971-09-5, Vinpocetine 43033-72-3, Levomethadyl acetate hydrochloride 43143-11-9, Bispyrithione magsulfex 43200-80-2, Zopiclone 43210-67-9, Fenbendazole 47141-42-4, Levobunolol 49562-28-9, Fenofibrate 49637-08-3, Nabitan hydrochloride 49697-38-3, Rimexolone 49755-67-1, Ioglicic acid 49763-96-4, Stiripentol 49780-10-1, Azaclorzine hydrochloride 49847-97-4, Prorenoate potassium 50264-69-2, Lonidamine 50370-12-2, Cefadroxil 50528-97-7, Xilobam 50650-76-5, Piroctone 50673-97-7, Colestolone 50679-07-7, Cinepazet maleate 50679-08-8, Terfenadine 50700-72-6, Vecuronium bromide 50708-95-7, Tinabinol 50838-36-3, Tolciclate 50847-11-5, Ibudilast 50924-49-7, Mizoribine 51022-71-0, Nabilone 51022-73-2, Zometapine 51022-74-3, Iotroxic acid 51022-75-4, Cliprofen 51022-76-5, Sulnidazole 51022-98-1, Butirosin sulfate 51025-85-5, Arbekacin 51222-36-7, Ciclafrine hydrochloride 51222-37-8, Iproxamine hydrochloride 51234-28-7, Benoxaprofen 51264-14-3, Amsacrine 51321-79-0, Sparfosic acid 51333-22-3, Budesonide 51354-31-5, Nisterime acetate 51384-51-1, Metoprolol 51481-61-9, Cimetidine 51481-63-1, Bucainide maleate 51481-65-3, Mezlocillin 51481-67-5, Octriptyline phosphate 51598-60-8, Cimetropium bromide 51627-14-6, Cefatrizine 51627-20-4, Cefaparole 51762-05-1, Cefroxadine 51764-33-1, Iodoxamate meglumine 51773-92-3, Mefloquine hydrochloride

51781-06-7, Carteolol 51781-21-6, Carteolol hydrochloride 51876-98-3, Gliamilide 51876-99-4, Ioseric acid 52123-49-6, Cefazaflur sodium 52128-35-5, Trimetrexate 52212-02-9, Pipecuronium bromide 52214-84-3, Ciprofibrate 52279-58-0, Metogest 52279-59-1, Moxnidazole 52365-63-6, Dipivefrin 52389-27-2, Dexclamol hydrochloride 52468-60-7, Flunarizine 52618-68-5, Tioperidone hydrochloride 52645-53-1, Permethrin 52663-86-2 52760-47-1, Tametraline hydrochloride 52794-97-5, Carubicin hydrochloride 53066-26-5, Lexithromycin 53123-88-9, Sirolimus 53152-21-9, Buprenorphine hydrochloride 53179-07-0, Nisoxetine 53179-10-5, Fluperamide 53179-12-7, Clopimozide 53179-13-8, Pirfenidone 53267-01-9, Cibenzoline 53361-24-3, Imafen hydrochloride 53400-68-3, Tiquinamide hydrochloride 53583-79-2, Sultopride 53597-26-5, Etoformin hydrochloride 53597-27-6, Fendosal 53597-28-7, Fludazonium chloride 53643-48-4, Vindesine 53648-55-8, Dezocine 53714-56-0, Leuprolide 53716-45-3, Anilopam hydrochloride 53716-47-5, Nexeridine hydrochloride 53716-49-7, Carprofen 53716-50-0, Oxfendazole 53736-52-0, Cromitrile sodium 53808-87-0, Tetroxoprim 53808-88-1, Lonazolac 53902-12-8, Tranilast 53910-25-1, Pentostatin 53983-00-9, Nibroxane 53994-73-3, Cefaclor 54024-22-5, Desogestrel 54048-10-1, Etonogestrel 54081-68-4, Vinleurosine sulfate 54120-61-5, Prostalene 54143-54-3, Sepazonium chloride 54143-55-4, Flecainide 54182-58-0, Sucralfate 54182-60-4 54194-00-2, Salcolex 54239-37-1, Cimaterol 54350-48-0, Etretinate 54504-70-0, Theofibrate 54527-84-3, Nicardipine hydrochloride 54573-75-0, 1α-hydroxyvitamin D2 54605-45-7, Iocarmate meglumine 54644-15-4 54739-18-3, Fluvoxamine 54767-75-8, Suloctidil 54824-17-8, Mitonafide 54910-89-3, Fluoxetine 54965-22-9, Fluspiperone 55028-70-1, Arbaprostil 55028-71-2, Fluprostenol sodium 55028-72-3 55096-26-9, Nalmefene 55134-13-9, Narasin 55142-85-3, Ticlopidine 55149-05-8, Pirolate 55162-26-0, Pirbenicillin sodium 55242-55-2, Propentofylline 55242-74-5, Oxifungin hydrochloride 55242-77-8, Triafungin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release active ingredients)

IT 55268-75-2, Cefuroxime 55294-15-0, Muzolimine 55298-68-5, Neomycin palmitate 55453-87-7, Isoxepac 55560-96-8, Tixocortol pivalate 55694-87-6, Pentizidone sodium 55695-56-2, Cloroperone hydrochloride 55721-11-4, Secalciferol 55774-33-9, Azathioprine sodium 55779-18-5, Arprinocid 55837-27-9, Piretanide 55837-29-1, Tiropramide 55870-64-9, Pentisomicin 55881-07-7, Miokamycin 55905-53-8, Clebopride 55981-09-4, Nitazoxanide 56030-54-7, Sufentanil 56049-88-8, Indacrinone 56079-80-2, Ropitoin hydrochloride 56093-45-9, Selenium sulfide 56119-96-1, Furodazole 56187-89-4, Ximoprofen 56208-01-6, Pifarnine 56211-40-6, Torasemide 56219-57-9, Arildone 56281-36-8, Motretinide 56290-94-9, Medroxalol 56383-05-2, Zindotrine 56391-55-0, Octazamide 56391-57-2, Netilmicin sulfate 56420-45-2, Epirubicin 56430-99-0, Flumecinol 56470-64-5, Anordrin 56605-16-4D, Spiromustine, di-Ph derivs. 56611-65-5, Oxagrelate 56689-42-0, Repromicin 56689-44-2, Nitramisole hydrochloride 56717-18-1, Isotiquimide 56741-95-8, Bropirimine 56784-39-5, Ozolinone 56796-20-4, Cefmetazole 56917-29-4, Fluretofen 56980-93-9, Celiprolol 56995-20-1, Flupirtine 57010-32-9, Tiapamil hydrochloride 57041-67-5, Desflurane 57067-46-6, Isamoxole 57109-90-7, Clorazepate dipotassium 57149-07-2, Naftopidil 57166-13-9, Napactadine hydrochloride 57248-88-1, Pamidronate disodium 57262-94-9, Setiptiline 57285-09-3, Folliculostatin 57381-26-7, Irsogladine 57432-61-8, Methylergonovine maleate 57441-90-4, Nivimedone sodium 57540-79-1, Nisbuterol mesylate 57645-05-3, Sermetacin 57653-26-6, Fenobam 57666-60-1, Nitrafudam hydrochloride 57726-65-5, Nufenoxole 57773-63-4, Triptorelin 57773-65-6, Deslorelin 57775-22-1, Etoperidone hydrochloride 57781-15-4, Halopredone 57801-81-7, Brotizolam 57808-65-8, Closantel 57982-78-2, Budipine 57998-68-2, Diaziquone 58019-50-4, Menabitan hydrochloride 58019-65-1, Nabazenil 58066-85-6, Miltefosine 58152-03-7, Isepamicin 58167-78-5, Tandamine hydrochloride 58239-89-7, Moxazocine 58261-91-9, Mefenidil 58473-74-8, Cinromide 58493-49-5, Olvanil 58497-00-0, Procinonide 58503-79-0, Meobentine sulfate 58524-83-7, Ciprocinonide 58525-82-9, Azatyrosine 58581-89-8, Azelastine 58712-69-9, Traxanox 58795-03-2, Apalcillin sodium 58934-46-6, Lorcainide hydrochloride 58944-73-3, Sinefungin

58957-92-9, Idarubicin 58970-76-6, Ubenimex 59017-64-0, Ioxaglic acid 59018-13-2 59070-06-3, Ticarcillin cresyl sodium 59122-46-2, Misoprostol 59160-29-1, Lidofenin 59170-23-9, Bevantolol 59179-95-2, Lorzafone 59227-89-3, Laurocapram 59263-76-2, Meptazinol hydrochloride 59333-90-3, Exaprolol hydrochloride 59467-96-8, Midazolam hydrochloride 59497-39-1, Naflocort 59653-73-5, Teroxirone 59703-84-3, Piperacillin sodium 59729-33-8, Citalopram 59733-86-7, Butikacin 59756-39-7, Enolicam sodium 59794-18-2, Paulomycin 59803-98-4, Brimonidine 59804-37-4, Tenoxicam 59831-63-9, Doconazole 59831-64-0, Milenperone 59831-65-1, Halopemide 59917-39-4, Vindesine sulfate 59937-28-9, Malotilate 59954-01-7, Pamatolol sulfate 60019-19-4, Iotetric acid 60050-95-5, Sulfoxamine 60084-10-8, Tiazofurin 60086-22-8, Clopipazan mesylate 60135-22-0, Flumoxonide 60142-96-3, Gabapentin 60166-93-0, Iopamidol 60200-06-8, Clorsulon 60207-31-0, Azaconazole 60209-20-3, Lycetamine 60282-87-3, Gestodene 60325-46-4, Sulprostone 60398-23-4, Iodoamiloride 60400-92-2, Proxicromil 60525-15-7, Zimelidine hydrochloride 60560-33-0, Pinacidil 60569-19-9, Propiverine 60607-34-3, Oxatomide 60607-35-4, Topterone 60628-96-8, Bifonazole 60653-25-0, Orpanoxin 60719-84-8, Amrinone 60719-85-9, Ciprefadol succinate 60762-57-4, Pirlindole 60857-08-1, Prostratin 60925-61-3, Ceforanide 60940-34-3, Ebselen 60976-05-8 61036-62-2, Teicoplanin 61177-45-5, Clavulanate potassium 61220-69-7, Tiopinac 61260-05-7, Prenalterol hydrochloride 61263-35-2, Meteneprost 61270-78-8, Cefonicid sodium 61318-91-0, Sulconazole nitrate 61325-80-2, Flumezapine 61379-65-5, Rifapentine 61380-27-6, Carfentanil citrate 61380-41-4, Lofentanil oxalate 61413-54-5, Rolipram 61444-62-0, Nifluridide 61477-94-9, Pirmenol hydrochloride 61481-30-9, Dicranin 61484-39-7, Pareptide sulfate 61489-71-2, Menotropin 61570-90-9, Tioxidazole 61622-34-2, Cefotiam 61825-94-3, Oxaliplatin 61849-14-7, Epoprostenol sodium 61869-08-7, Paroxetine 62013-04-1, Dirithromycin 62087-72-3, Pentigetide 62134-34-3, Butoprozine hydrochloride 62220-58-0, Bipenamol hydrochloride 62265-68-3, Quinfamide 62304-98-7, Thymalfasin 62435-42-1, Perfosfamide 62488-57-7 62571-86-2, Captopril 62571-87-3, Minaxolone 62587-73-9, Cefsulodin 62613-82-5, Oxiracetam 62625-19-8, Pirogliride tartrate 62658-63-3, Bopindolol 62666-20-0, Progabide 62732-44-9, Ipidacrine 62816-98-2, Ormaplatin 62851-43-8, Zidometacin 62893-20-3, Cefoperazone sodium 62928-11-4, Iproplatin 62929-91-3, Procaterol hydrochloride 62973-76-6, Azanidazole 62973-77-7, Parconazole hydrochloride 62989-33-7, Sapropterin 62996-74-1, Staurosporine 63119-27-7, Anitrazafen 63198-97-0, Viroxime 63204-23-9, Oxmetidine hydrochloride 63245-28-3, Etifenin 63251-39-8, Sulfinalol hydrochloride 63269-31-8, Ciramadol 63358-49-6, Aspoxicillin 63534-64-5, Iosulamide meglumine 63585-09-1, Foscarnet sodium 63590-19-2, Balanol 63590-64-7, Terazosin 63612-50-0, Nilutamide 63659-18-7, Betaxolol 63659-19-8, Betaxolol hydrochloride 63675-72-9, Nisoldipine 63774-77-6, Somatomedin B 63941-73-1, Ioglucol 63941-74-2, Ioglucomide 63950-06-1, Esorubicin hydrochloride 64019-93-8, Dipivefrin hydrochloride 64059-66-1, Cetaben sodium 64063-83-8, Picotrin diolamine 64092-48-4, Zomepirac sodium 64211-45-6, Oxiconazole 64221-86-9, Imipenem 64228-81-5, Atracurium besylate 64318-79-2, Gemeprost 64379-93-7, Cinflumide 64420-40-2, Etibendazole 64461-82-1, Tizanidine hydrochloride 64485-93-4, Cefotaxime sodium 64706-54-3, Bepridil 64808-48-6, Lobenzarit sodium 64872-77-1, Butoconazole nitrate 64924-67-0, Halofuginone hydrobromide 64953-12-4, Moxalactam disodium 65009-35-0, Lidamidine hydrochloride 65043-22-3, Indeloxazine hydrochloride 65052-63-3, Cefetamet 65057-90-1, Talisomycin 65093-40-5, Cytarabine ocfosfate 65141-46-0, Nicorandil 65222-35-7, Pazelliptine 65271-80-9, Mitoxantrone 65277-42-1, Ketoconazole 65322-72-7, Endralazine mesylate 65454-13-9, Lateritin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release active ingredients)

IT 65473-14-5, Naftifine hydrochloride 65511-42-4, Nantradol hydrochloride 65573-02-6, Impromidine hydrochloride 65646-68-6, Fenretinide 65652-44-0, Pirbuterol acetate 65717-97-7, Disofenin 65807-02-5, Goserelin 65847-85-0, Morniflumate 65886-71-7, Fazarabine 65899-73-2, Tioconazole 65928-58-7, Dienogest 65950-99-4, Pirquinozol 66085-59-4, Nimodipine 66104-22-1, Pergolide 66108-95-0, Iohexol

66148-78-5, Temocillin 66172-75-6, Verofylline 66195-31-1, Ibopamine 66292-52-2, Butilfenin 66292-53-3, Iprofenin 66357-35-5, Ranitidine 66357-59-3, Zantac 66364-74-7, Enpiroline phosphate 66504-75-4, Bicifadine hydrochloride 66537-94-8, Cyproximide 66564-14-5, Cinitapride 66569-27-5, Sparfosate sodium 66575-29-9, Colforsin 66608-04-6, Rolgamidine 66635-85-6, Anirolac 66711-21-5, Apraclonidine 66722-44-9, Bisoprolol 66734-12-1, Butopamine 66849-34-1, Dexifosfamide 66852-54-8, Halobetasol propionate 66887-96-5, Propikacin 66898-60-0, Talosalate 66898-62-2, Talniflumate 66960-35-8, Metkephamid acetate 66969-81-1, Tiodazosin 67102-87-8, Pentomone 67227-55-8, Primidolol 67227-56-9, Fenoldopam 67337-44-4, Sarmoxicillin 67394-31-4, Verilopam hydrochloride 67422-14-4, Proinsulin (human) 67450-45-7, Eclanamine maleate 67489-39-8, Talmetacin 67699-41-6, Vinzolidine sulfate 67700-30-5, Furaprofen 67763-96-6, Somatomedin C 67832-40-0, Malethamer 67915-31-5, Terconazole 67992-58-9 68099-86-5, Bepridil hydrochloride 68252-19-7, Pirmenol 68284-69-5, Disobutamide 68291-97-4, Zonisamide 68302-57-8, Amlexanox 68307-81-3, Trioxifene mesylate 68367-52-2, Sorbinil 68377-92-4, Arotinolol 68379-03-3, Clofilium phosphate 68401-82-1, Ceftizoxime sodium 68475-42-3, Anagrelide 68506-86-5, Vigabatrin 68616-83-1, Pentamorphone 68630-75-1, Buserelin acetate 68681-42-5, Tonazocine mesylate 68693-11-8, Modafinil 68693-30-1, Somantadine hydrochloride 68741-18-4, Buterizine 68813-55-8, Oxantel pamoate 68844-77-9, Astemizole 68902-57-8, Metioprim 69014-14-8, Tiotidine 69049-73-6, Nedocromil 69123-90-6, Fiacitabine 69123-98-4, Fialuridine 69207-52-9, Methyl palmoxirate 69365-67-9, Fenoctimine sulfate 69372-19-6, Pemirolast 69376-27-8, Dextrorphan hydrochloride 69381-94-8, Fenprostalene 69388-79-0, Sulbactam pivoxil 69402-03-5, Piridicillin sodium 69425-13-4, Prifelone 69429-85-2, Cilobamine mesylate 69598-75-0, Complestatin 69648-38-0, Butaprost 69655-05-6, Didanosine 69712-56-7, Cefotetan 69739-16-8, Cefodizime 69756-53-2, Halofantrine 69815-39-0, Proxorphan tartrate 69839-83-4, Didox 69900-72-7, Trimoprostil 70018-51-8, Quazinone 70052-12-9, Eflornithine 70169-80-1, Lofemizole hydrochloride 70222-86-5, Levonantradol hydrochloride 70288-86-7, Ivermectin 70374-27-5, Lomoxicam 70374-39-9, Lornoxicam 70384-29-1, Peplomycin sulfate 70384-91-7, Lortalamine 70458-92-3, Pefloxacin 70458-96-7, Norfloxacin 70529-35-0, Itazigrel 70590-58-8, Etrabamine 70641-51-9, Edelfosine 70704-03-9, Vinconate 70724-25-3, Carbazeran 70775-75-6, Octenidine hydrochloride 70788-28-2, Flurofamide 70788-29-3, Tolfamide 70797-11-4, Cefpiramide 70801-02-4, Flutroline 70865-14-4, Conorphone hydrochloride 70891-37-1, Nafimidone hydrochloride 70895-39-5, Tipropidil hydrochloride 70931-18-9, Isofloxythepin 71002-09-0, Pirazolac 71119-11-4, Bucindolol 71144-97-3, Probicromil calcium 71251-04-2, Surfomer 71276-44-3, Quadazocine mesylate 71294-60-5, Rohitukine 71320-77-9, Moclobemide 71351-79-6, Icotidine 71486-22-1, Vinorelbine 71522-58-2, Forfenimex 71576-41-5, Aptazapine maleate 71628-96-1, Menogaril 71653-63-9, Riodipine 71675-85-9, Amisulpride 71678-03-0, Illimaquinone 71767-13-0, Iotasul 71807-56-2, Etintidine hydrochloride 72238-02-9D, Retelliptine, demethylated 72275-67-3, Astromicin sulfate 72301-78-1, Zinviroxime 72301-79-2, Enviroxime 72318-55-9, Indorenate hydrochloride 72324-18-6, Stepronin 72432-03-2, Miglitol 72432-10-1, Aniracetam 72479-26-6, Fenticonazole 72481-99-3, Brocrinat 72496-41-4, Pirarubicin 72509-76-3, Felodipine 72558-82-8, Ceftazidime 72559-06-9, Rifabutin 72573-82-1, Gadoteric acid 72629-69-7, Sarcophytol A 72702-95-5, Ponalrestat 72732-56-0, Piritrexim 72741-87-8, Swainsonine 72797-41-2, Tianeptine 72803-02-2, Darodipine 72808-81-2, Tepirindole 72822-12-9, Dapiprazole 72895-88-6, Eltenac 72956-09-3, Carvedilol 73080-51-0, Repirinast 73105-03-0, Pentamustine 73196-97-1, Dactimicin 73205-13-7, Ticabesone propionate 73218-79-8, Apraclonidine hydrochloride 73231-34-2, Florfenicol 73247-43-5, Gonadocrinin 73264-44-5, Sucrosofate potassium 73334-07-3, Iopromide 73384-59-5, Ceftriaxone 73514-87-1, Fosarilate 73573-87-2, Formoterol 73590-58-6, Omeprazole 73647-73-1, Viprostol 73681-12-6, Indecainide hydrochloride 73747-21-4, Naboctate hydrochloride 73771-04-7, Prednicarbate 73793-66-5, Prizidilol hydrochloride 73803-48-2, Tripamide 73899-76-0, Diacetolol hydrochloride 73963-72-1, Cilostazol 74011-58-8, Enoxacin 74014-51-0, Rokitamycin 74050-98-9, Ketanserin 74103-06-3, Ketorolac

74129-03-6, Tebuquine 74149-70-5, Parabactin 74150-27-9, Pimobendan
74226-22-5, Dazoxiben hydrochloride 74381-53-6, Leuprolide acetate
74434-21-2, Cucumarioside 74513-62-5, Trimegestone 74559-85-6,
Zenazocine mesylate 74639-40-0, Docarpamine 74711-43-6, Zaltoprofen
74738-24-2, Recainam 74752-07-1, Recainam hydrochloride 74772-77-3,
Ciglitazone 74790-08-2, Spiroplatin 74863-84-6, Argatroban
75067-66-2, Bromperidol decanoate 75176-37-3, Zofenoprilat 75219-46-4,
Atrimustine 75330-75-5, Lovastatin 75358-37-1, Linogliride
75438-57-2, Moxonidine 75444-64-3, Flumeridone 75444-65-4, Pirenperone
75530-68-6, Nilvadipine 75564-40-8, Biclodil hydrochloride 75607-67-9,
Fludarabine phosphate 75659-08-4, Dilevalol hydrochloride 75689-38-2,
Piquindone hydrochloride 75695-93-1, Isradipine 75696-02-5,
Cinolazepam 75733-50-5, Pramiracetam hydrochloride 75738-58-8,
Cefmenoxime hydrochloride 75751-89-2, Iogulamide 75847-73-3, Enalapril
75859-03-9, Rimcazole hydrochloride 75889-62-2, Fostedil 75957-60-7,
Splenopentin 75991-49-0, Dazepinil hydrochloride 76053-16-2,
Reclazepam 76144-81-5, Mildronate 76168-82-6, Ramoplanin 76263-13-3,
Fluzinamide 76301-19-4, Timefurone 76420-72-9, Enalaprilat
76448-47-0, Veradoline hydrochloride 76470-66-1, Loracarbef
76497-13-7, Sultamicillin 76535-71-2, Suproclone
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release
active ingredients)

IT 76541-72-5, Mifobate 76547-98-3, Lisinopril 76568-02-0, Flosequinan
76584-70-8, Depakote 76610-84-9, Cefbuperazone 76712-82-8, Histrelin
76824-35-6, Famotidine 76894-77-4, Dazmegrel 76932-56-4, Nafarelin
76963-41-2, Axid 76990-56-2, Milacemide 77016-85-4, Plomestane
77086-22-7, Dizocilpine maleate 77164-20-6, Levomoprolol 77181-69-2,
Sorivudine 77257-42-2, Stilonium iodide 77287-05-9, Rioprostil
77287-90-2, Xorphanol mesylate 77327-05-0, Didemnin B 77590-95-5,
Cetamolol hydrochloride 77590-96-6, Flordipine 77590-97-7, Fluradoline
hydrochloride 77599-17-8, Panomifene 77671-31-9, Enoximone
77679-27-7 77858-21-0, Velaresol 78013-07-7, Bactobolamine
78040-85-4, Coumermycin 78110-38-0, Aztreonam 78113-36-7, Romurtide
78186-33-1, Fumoxicillin 78186-34-2, Bisantrene 78266-06-5, Mebrofenin
78273-80-0, Roxatidine 78299-53-3, Tiacrilast 78308-51-7 78371-66-1,
Bucromarone 78415-72-2, Milrinone 78613-35-1, Amorolfine 78649-41-9,
Iomeprol 78755-81-4, Flumazenil 78822-40-9, Pirlimycin hydrochloride
78860-34-1, (L-783281) 78919-13-8, Iloprost 78967-07-4, Mofezolac
78994-23-7, Levormeloxifene 79094-20-5, Daltroban 79201-85-7,
Picenadol 79211-34-0, Iotriside 79217-60-0, Cyclosporin 79350-37-1,
Cefixime 79404-91-4, Cilofungin 79498-31-0, Glaucocalyxin A
79516-68-0, Levocabastine 79578-14-6, Timobesone acetate 79617-96-2,
Sertraline 79619-32-2, Flavodilol maleate 79660-72-3, Fleroxacin
79672-88-1, Piriprost 79712-53-1, Tazifylline hydrochloride
79770-24-4, Iotrolan 79778-41-9, Neridronic acid 79794-75-5,
Loratadine 79798-39-3, Ketorfanol 79831-76-8, Castanospermine
79874-76-3, Delmopinol 79902-63-9, Simvastatin 80018-06-0, Fengabine
80125-14-0, Remoxipride 80168-44-1, Zinoconazole hydrochloride
80195-36-4, Cefdaloxime 80214-83-1, Roxithromycin 80263-73-6,
Eclazolast 80343-63-1, Sufotidine 80410-37-3, Fezolamine fumarate
80433-71-2, Levoleucovorin calcium 80451-05-4, Cecropin B 80474-14-2,
Fluticasone propionate 80486-69-7, Cloticasone propionate 80573-04-2,
Balsalazide 80576-83-6, Edatrexate 80621-81-4, Rifaximin 80755-51-7,
Bunazosin 80809-81-0, Docebenone 80828-32-6, Indolapril hydrochloride
80841-47-0, Asulacrine 80879-63-6, Emiglitate 80880-90-6, Telenzepine
80883-55-2, Enviradene 81026-63-3, Enisoprost 81045-50-3, Pivopril
81093-37-0, Pravastatin 81098-60-4, Propulsid 81103-11-9,
Clarithromycin 81129-83-1, Cilastatin sodium 81131-70-6, (Pravachol)
81161-17-3, Esmolol hydrochloride 81167-22-8, Imiloxan hydrochloride
81329-71-7, Modecainide 81377-02-8, L 363586 81382-52-7, Pentiapine
maleate 81424-67-1, Caracemide 81435-67-8, Losulazine hydrochloride
81447-80-5, Diprafenone 81447-81-6, Bromadoline maleate 81525-10-2,
Nafamostat 81669-57-0, Anistreplase 81732-65-2, Bambuterol
81737-62-4, Bendacalol mesylate 81801-12-9, Xamoterol 81840-15-5,
Vesnarinone 81845-44-5, Ciprostene 81907-78-0, Batebulast
81938-43-4, Zofenopril calcium 81957-25-7, Dazopride fumarate
81965-43-7, Sarcnu 82030-87-3, Somatrem 82101-10-8, Flerobuterol
82186-77-4, Benflumetol 82230-03-3, Carbetimer 82230-53-3, Girisopam

82239-52-9, Moxiraprine 82248-59-7, Tomoxetine hydrochloride
82410-32-0, Ganciclovir 82419-36-1, Ofloxacin 82547-58-8, Cefteram
82571-53-7, Ozagrel 82626-48-0, Zolpidem 82664-20-8, Flurithromycin
82707-54-8, Neutral endopeptidase 82708-31-4, Oocyte maturation
inhibitor 82752-99-6, Nefazodone hydrochloride 82768-85-2, Quinaprilat
82834-16-0, Perindopril 82855-09-2D, Combretastatin, analogs
82857-82-7, Ilepcimide 82924-03-6, Pentopril 82964-04-3, Tolrestat
82989-25-1, Tazanolast 83059-56-7, Zabicipril 83086-73-1, Tubulozole
hydrochloride 83150-76-9, Octreotide 83166-18-1, Tampramine fumarate
83198-90-7, Tiprinast meglumine 83200-11-7, Vinepidine sulfate
83435-66-9, Delapril 83435-67-0, Delapril hydrochloride 83462-55-9,
Deoxypyridinoline 83519-04-4, Ilmofosine 83529-09-3, Ciladopa
hydrochloride 83602-05-5, Spiraprilat 83646-97-3, Inocoterone
83688-84-0, Tertatolol 83784-18-3, Lutrelin acetate 83799-24-0,
Fexofenadine 83805-11-2, Flocalcitriol 83863-79-0, Florifenine
83881-51-0, Cetirizine 83898-67-3, Mioflazine hydrochloride
83905-01-5, Azithromycin 83928-76-1, Gepirone 83997-75-5,
Iododoxorubicin 84057-84-1, Lamotrigine 84057-95-4, Ropivacaine
84088-42-6, Roquinimex 84166-17-6, Fenprinast hydrochloride
84203-09-8, Trifenagrel 84290-27-7, Tucaresol 84305-41-9, Cefminox
84371-65-3, Mifepristone 84379-13-5, Bretazenil 84392-17-6, Xenalipin
84408-37-7, Desciclovir 84412-94-2, Ruboxyl 84449-90-1, Raloxifene
84485-00-7, Sibutramine hydrochloride 84490-12-0, Piroximone
84611-23-4, Erdosteine 84625-61-6, Itraconazole 84845-57-8, Ritipenem
84845-75-0, Niperotidine 84880-03-5, Cefpimizole 84957-29-9, Cefpirome
85053-47-0, Suricainide maleate 85068-76-4 85118-44-1, Minocromil
85136-71-6, Tilisolol 85175-67-3, Zatebradine 85181-38-0, Tropanserin
hydrochloride 85197-77-9, Tipredane 85202-17-1, Stobadine 85216-79-1
85441-61-8, Quinapril 85465-82-3, Thymotrinan 85468-01-5, Gusperimus
trihydrochloride 85622-93-1, Temozolomide 85650-52-8, Mirtazapine
85666-17-7, Furegrelate sodium 85683-41-6, Metipamide 85691-74-3,
Pirmagrel 85721-33-1, Ciprofloxacin 85798-08-9, Quinpirole
hydrochloride 85969-07-9, Budotitane 85977-49-7, Tauromustine
86015-38-5, Neflumozide hydrochloride 86042-50-4, Cistinexine
86048-40-0, Quazolast 86050-77-3, Gadopentetate dimeglumine
86116-60-1, Azaloxan fumarate 86160-82-9, Lavoltidine succinate
86181-42-2, Temelastine 86386-73-4, Fluconazole 86433-40-1,
Terflavoxate 86487-64-1, Setoperone 86541-74-4, Benazepril
hydrochloride 86541-78-8, Benazeprilat 86780-90-7, Aranidipine
86828-07-1, Mallotojaponin 86832-68-0, Carumonam sodium 86914-11-6,
Tolgabide 87005-03-6, Panaxytriol 87051-43-2, Ritanserin 87056-78-8,
Quinagolide 87071-16-7, Arclofenin 87173-97-5, Spiradoline mesylate
87233-61-2, Emedastine 87239-81-4, Cefpodoxime proxetil 87248-13-3,
Vapiprost hydrochloride 87333-19-5, Ramipril 87359-33-9, Isomazole
hydrochloride 87495-31-6, Disoxaril 87495-33-8, Napamezole
hydrochloride 87573-01-1, Salnacedin 87638-04-8, Carumonam
87679-37-6, Trandolapril 87691-92-7, Tiospirone hydrochloride
87719-32-2, Etarotene
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release
active ingredients)

IT 87726-17-8, Panipenem 87760-53-0, Tandospirone 87771-40-2, Ioversol
87784-12-1, Ofornine 87806-31-3, Porfimer sodium 87810-56-8,
Fostriecin 87936-82-1, Tazadolene succinate 88040-23-7, Cefepime
88069-67-4, Pilsicainide 88107-10-2, Tomelukast 88133-11-3,
Bemitradine 88150-42-9, Amlodipine 88296-61-1, Medorinone
88296-62-2, Transcainide 88303-60-0, Losoxantrone 88430-50-6,
Beraprost 88637-37-0, Diphenhydramine citrate 88669-04-9,
Trospectomycin 88768-40-5, Cilazapril 88844-73-9, Flestolol sulfate
89194-77-4, Bisaramil 89198-09-4, Imazodan hydrochloride 89213-87-6,
Carperitide 89226-50-6, Manidipine 89232-84-8, Pelrinone hydrochloride
89303-64-0, Atiprosin maleate 89365-50-4, Salmeterol 89371-37-9,
Imidapril 89383-13-1, Somidobove 89419-40-9, Mosapramine 89565-68-4,
Tropisetron 89651-00-3, Voxergolide 89667-40-3, Isbogrel 89672-11-7,
Cioteronel 89778-26-7, Toremifene 89786-04-9, Tazobactam 89797-00-2,
Iopentol 89943-82-8, Cicletanine 89987-06-4, Tiludronic acid
90055-97-3, Tienoxolol 90182-92-6, Zacopride 90243-66-6, Montirelin
90274-23-0, Zaltidine hydrochloride 90293-01-9, Bifemelane 90357-06-5,
Bicalutamide 90729-41-2, Oxodipine 90729-43-4, Ebastine 90733-42-9,

Edifolone acetate 90779-69-4, Atosiban 90849-08-4, Oximonam sodium 90850-05-8, Gloximonam 90898-90-1, Oximonam 90996-54-6, Rhizoxin 91077-32-6, Dezinamide 91161-71-6, Terbinafine 91296-86-5, Difloxacin hydrochloride 91296-87-6, Sarafloxacin hydrochloride 91374-21-9, Ropinirole 91406-11-0, Esuprone 91431-42-4, Lonapalene 91524-15-1, Irloxacin 91524-18-4, Azumolene sodium 91587-01-8, Pelretin 91618-36-9, Ibafloxacin 91714-94-2, Bromfenac 91832-40-5, Cefdinir 92047-76-2, Tetrachlorodecaoxide 92118-27-9, Fotemustine 92236-42-5, Glutapyrone 92339-11-2, Iodixanol 92623-84-2, Pravadoline maleate 92623-85-3, Milnacipran 92665-29-7, Cefprozil 92788-10-8, Rogletimide 92803-82-2, Aphidicolin glycinate 92812-82-3, fluorodopaf18 92817-10-2, 16-α-Fluoroestradiol 93047-39-3, Etanterol 93135-89-8, Methoxatone 93221-48-8, Levobetaxolol 93390-81-9, Fosphenytoin 93413-69-5, Venlafaxine 93479-97-1, Glimepiride 93738-40-0, Ralitoline 93957-54-1, Fluvastatin 93957-55-2, Fluvastatin sodium 94079-80-8, Cicaprost 94168-98-6, Rifametane 94535-50-9, Levcromakalim 94651-09-9, Cicloprolol 94739-29-4, Lemildipine 94820-09-4, Cadexomer iodine 94841-17-5, Spirapril hydrochloride 95058-81-4, Gemcitabine 95153-31-4, Perindoprilat 95190-13-9, Tetrazolast meglumine 95232-68-1, Tenosal 95233-18-4, Atovaquone 95399-71-6, Fosinoprilat 95522-45-5, Colestimide 95635-55-5, Ranolazine 95671-26-4, Tipentosin hydrochloride 95733-03-2, Daphnodorin A 95734-82-0, Nedaplatin 95847-70-4, Ipsapirone 95896-08-5, Anaritide 96036-03-2, Meropenem 96128-92-6, Clentiazem maleate 96201-88-6, Brequinar sodium 96301-34-7, Atamestane 96346-61-1, Onapristone 96389-68-3, Crisnatol 96392-96-0, Dexormaplatin 96449-05-7, Rispenzepine 96604-21-6, Ocinaplon 96609-16-4, Lifibrol 96736-12-8 96829-58-2, Orlipastat 96892-57-8, Hepsulfam 96946-42-8, Cisatracurium besilate 97048-13-0, Urofollitropin 97068-30-9, Elsamitrucin 97240-79-4, Topiramate 97322-87-7, Troglitazone 97519-39-6, Ceftibuten 97534-21-9, Merbarone 97548-97-5, Quinelorane hydrochloride 97682-44-5, Irinotecan 97772-98-0, Butedronate tetrasodium 97919-22-7 97938-30-2, Vexibinol 97964-56-2, Lorglumide 98048-97-6, Fosinopril 98079-51-7, Lomefloxacin 98116-53-1, Sulukast 98206-10-1, Flesinoxan 98319-26-7, Finasteride 98383-18-7, Ecomustine 98449-05-9, Butixocort propionate 98569-62-1, Mallotochromene 98631-95-9, Sobuzoxane 99009-20-8, Pyrazoloacridine 99011-02-6, Imiquimod 99107-52-5, Bunaprolast 99149-95-8, Saruplase 99156-66-8, Barmastine 99248-33-6, Seglitide acetate 99258-56-7, Oxamisole 99283-10-0, Molgramostim 99287-30-6, Egualen 99291-25-5, Levodropropizine 99294-94-7, Teriparatide acetate 99464-64-9, Ampiroxicam 99519-84-3, Carboxyamidotriazole 99592-32-2, Sertaconazole 99614-02-5, Ondansetron 99665-00-6, Flomoxef 99705-65-4, Naxagolide hydrochloride 99759-19-0, Tiqueside 99821-44-0, Nasaruplase 100188-33-8, Piridronate sodium 100324-81-0, Lisofylline 100427-26-7, Lercanidipine 100490-36-6, Tosufloxacin 100643-96-7, Indolidan 100981-43-9, Ebrotidine 100986-85-4, Levofloxacin 101001-34-7, Pamicogrel 101246-66-6, Phenserine 101246-68-8, Eptastigmine 101363-10-4, Rufloxacin 101477-55-8, Lomerizine 101526-83-4, Sematilide 101530-10-3, Lanoconazole 101828-21-1, Butenafine 102394-31-0, Otenzepad 102396-24-7, Jasplakinolide 102426-96-0, Paldimycin 102583-46-0, Detirelix acetate 102625-70-7, Pantoprazole 102669-89-6, Saterinone 102670-59-7, Batanopride hydrochloride 102676-47-1, Fadrozole 102767-28-2, Levetiracetam 102822-56-0, Mannostatin A 102908-59-8, Binospirone 102916-21-2, Tigemonam dicholine 103060-53-3, Daptomycin 103222-11-3, Vapreotide 103255-66-9, Pazinaclone 103336-05-6, Ditekiren 103337-74-2, Letrazuril 103379-03-9, Monatepil maleate 103420-77-5, Devazepide 103475-41-8, Tepoxalin 103486-79-9, Belfosdil 103541-15-7, Clausenamide 103577-45-3, Lansoprazole 103614-76-2, Halichondrin B 103628-46-2, Sumatriptan 103745-39-7, Fasudil 103775-10-6, Moexipril 103878-84-8, Lazabemide 103890-78-4, Lacidipine 103909-75-7, 22-Oxacalcitriol 104054-27-5, Atipamezole 104153-37-9, Rilopirox 104227-87-4, Famciclovir 104340-86-5, Leminoprazole 104383-17-7, Sabeluzole 104393-00-2, Pirazmonam sodium 104454-71-9, Ipenoxazone 104456-95-3, Cisconazole 104595-79-1, Anaritide acetate 104713-75-9, Barnidipine 104719-71-3, Lorcinadol 104775-36-2, Ecabapide 104987-11-3, Tacrolimus 105102-18-9, Tibenelast sodium 105102-22-5, Mometasone 105118-12-5, Piroxantrone hydrochloride 105149-04-0,

Osaterone 105182-45-4, Fluparoxan 105219-56-5, Apafant 105250-86-0, Ebiratide 105431-72-9, Linopirdine 105462-24-6, Risedronic acid 105567-83-7, Berefrine 105613-48-7, Exametazime 105615-58-5, Oxaunomycin 105687-93-2, Sumarotene 105705-89-3 105784-61-0, Temafloxacin hydrochloride 105806-65-3, Efegatran 105851-17-0, fludeoxyglucosef18 105889-45-0, Cefcapene pivoxil 105913-11-9, Plasminogen activator
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release active ingredients)

IT 105920-77-2, Camonagrel 105956-97-6, Clinafloxacin 105979-17-7, Benidipine 106243-16-7, Thioperamide 106266-06-2, Risperdal 106282-98-8, Somalapor 106400-81-1, Lometrexol 106463-17-6, Tamsulosin hydrochloride 106498-99-1, Vintoperol 106516-24-9, Sertindole 106560-14-9, Faropenem 106602-62-4, Amylin 106730-54-5, Olprinone 106861-44-3, Mivacurium chloride 107000-34-0, Zanoterone 107167-31-7, Lactivicin 107266-08-0, Carvotroline 107361-33-1, Enazadrem 107407-62-5, Nelezaprine maleate 107429-63-0, Lintopride 107703-78-6, Glemanserin 107724-20-9, Epoxymexrenone 107753-78-6, Zafirlukast 107793-72-6, Ioxilan 107868-30-4, Exemestane 107902-67-0, Tazofelone 108073-62-7, Carbazomycin C 108310-20-9, Pirodomast 108609-34-3, Lixazinone sulfate 108612-45-9, Mizolastine 108674-87-9, Sergolexole maleate 108700-03-4, Teludipine hydrochloride 108736-35-2, Lanreotide 108778-82-1, Beractant 108852-90-0, Nemorubicin 108945-35-3, Taprostene 109214-55-3, Libenzapril 109229-58-5, Englitazone 109543-76-2, Romazarit 109636-76-2, Prinomide tromethamine 109837-67-4, Cycloplatam 109889-09-0, Granisetron 110101-66-1, Tirilazad 110140-89-1, Ridogrel 110267-81-7, Amrubicin 110311-27-8, Sulofenur 110347-85-8, Selfotel 110588-56-2, Noberastine 110588-57-3, Saperconazole 110623-33-1, Suritozole 110690-43-2, Emitefur 110703-94-1, Zopolrestat 110845-89-1, Remiprostol 110871-86-8, Sparfloxacin 111011-63-3, Efonidipine 111025-46-8, Pioglitazone 111073-18-8, Nemazoline hydrochloride 111149-90-7, Lodelaben 111212-85-2, Ersofermin 111223-26-8, Ceronapril 111406-87-2, Zileuton 111490-36-9, Zeniplatin 111523-41-2, Enloplatin 111672-14-1, Rocastine hydrochloride 111686-79-4, Remacemide hydrochloride 111753-73-2, Satigrel 111786-07-3, Prinoxodan 111902-57-9, Temocapril 111974-60-8, Ritolukast 111974-69-7, Quetiapine 112018-00-5, Tebufelone 112018-01-6, Bemoradan 112192-04-8, Roxindole 112243-58-0, Gevotroline hydrochloride 112344-52-2, Flobufen 112362-50-2, Dalfopristin 112515-43-2, Topsentin 112522-64-2, Acetyldinaline 112573-73-6, Ecadotril 112733-06-9, Zenarestat 112809-51-5, Letrozole 112856-44-7, Losigamone 112859-71-9, Fluasterone 112885-41-3, Mosapride 112887-68-0, Raltitrexed 112893-26-2, Becliconazole 112922-55-1, Cericlamine 112924-45-5, Sinnabidiol 112964-97-3, Ocfentanil hydrochloride 112965-21-6, Calcipotriene 113082-98-7, Enalkiren 113102-19-5, Rifamexil 113108-86-4, Suronacrine maleate 113359-04-9, Cefozopran 113378-31-7, Semduramicin 113427-24-0, Epoetin alfa 113471-15-1 113558-15-9, baohuoside 1 113593-34-3, Flosatidil 113658-85-8, Trombodipine 113662-23-0, Gadobenic acid 113665-84-2, Clopidogrel 113775-47-6, Dexmedetomidine 113806-05-6, Olopatadine 113852-37-2, Cidofovir 113932-41-5, Tematropium methyl sulfate 113957-09-8, Cebaracetam 114030-44-3, Dexpemedolac 114084-78-5, Ibandronic acid 114118-91-1, Tirandalydigin 114285-68-6, Lentinan sulfate 114298-18-9, Zalospirone 114317-44-1, magainin 2 amide 114432-13-2, Fantofarone 114517-02-1, Fosquidone 114716-16-4, Pemedolac 114798-26-4, Losartan 114977-28-5, Docetaxel 115103-54-3, Tiagabine 115150-59-9, Antagonist G 115256-11-6, Dofetilide 115308-98-0, Tallimustine 115436-72-1, Risedronate sodium 115436-73-2, Ipazilide 115566-02-4, Bistratene A 115575-11-6, Liarozole 115743-28-7, Curdlan sulfate 115762-17-9, Ruzadolane 115956-12-2, Dolasetron 116057-75-1, Idoxifene 116078-65-0, Bidisomide 116287-14-0, Lanperisone 116290-93-8, Hatomamicin 116313-94-1, Nitecapone 116476-13-2, Semotiadil 116523-57-0 116644-53-2, Mibefradil 116649-85-5, Ramatroban 116666-63-8, Mibefradil dihydrochloride 116684-92-5, Galdansetron 116818-99-6, Isalsteine 116853-25-9, Cefluprenam 116907-13-2, Risotilide hydrochloride 117048-59-6, combretastatin A4 117086-68-7, Ricasetron 117211-03-7, Cefetecol 117268-95-8, Brifentanil

hydrochloride 117467-28-4, Cefditoren pivoxil 117523-47-4, Mirfentanil
117545-11-6, Bimakalim 117581-05-2, Serazapine hydrochloride
117827-81-3, Delfaprazine 117857-45-1, Loreclezole 117946-91-5,
Luzindole 117976-90-6, Rabeprazole sodium 118072-93-8, Zoledronic acid
118288-08-7, Lafutidine 118292-40-3, Tazarotene 118353-05-2, Carbovir
118395-73-6, Chloroorienticin A 118457-14-0, Nebivolol 118635-52-2,
Tilnoprofen arbamel 118909-22-1, Velnacrine maleate 119006-77-8,
Flutrimazole 119129-70-3, Ananain 119169-78-7, Epristeride
119257-34-0, Besipirdine 119302-91-9, Rocuronium bromide 119413-54-6,
Topotecan hydrochloride 119413-55-7, Elgodipine 119422-08-1
119431-25-3, Eliprodil 119509-26-1, Atpenin B 119514-66-8, Lifarizine
119625-78-4, Terlakiren 119683-68-0, Ferumoxides 119693-74-2,
Somenopor 119758-39-3, Maduramicin 119813-10-4, Carzelesin
119817-90-2, Dexloxiglumide 119905-05-4, Delequamine 119914-60-2,
Grepafloxacin 120066-54-8, Gadoteridol 120128-20-3, RG 12525
120138-50-3, Quinupristin 120210-48-2, Tenidap 120287-85-6, Cetrorelix
120360-10-3, Batelapine maleate 120373-24-2, Isopropyl unoprostone
120410-24-4, Biapenem 120443-16-5, Verlukast 120444-71-5, Deramciclane
120500-15-4, Leinamycin 120511-73-1, Anastrozole 120551-59-9,
Crilvastatin 120635-25-8, Mofegiline hydrochloride 120635-74-7,
Cilansetron 120656-93-1, Trefentanil hydrochloride 120685-11-2,
Benzoylstaurosporine 120788-07-0, Sulopenem 120824-08-0, Linotroban
120993-53-5, Desirudin 121181-53-1, Filgrastim 121249-14-7,
Corticorelin ovine triflutate 121263-19-2, Calphostin C 121281-41-2,
technetium Tc 99 m bicisate 121288-39-9, Loxoribine 121547-04-4,
Mirimostim 121650-80-4, Pancopride 121679-13-8, Naratriptan
121749-39-1 121808-62-6, Pidotimod 121929-46-2, Zoniclezole
hydrochloride 122312-54-3, Epoetin beta 122341-38-2, Temoporfin
122431-96-3 122535-63-1, α-Citreamicin 122566-70-5, Maniwamycin
A 122575-28-4, Naglivan 122647-32-9, Ibutilide fumarate 122841-10-5,
Cefoselis 122898-63-9, Phenazinomycin 122898-67-3, Itopride
122946-43-4, Telmesteine 122955-18-4, Sibopirdine 123039-93-0,
Dihydrexidine 123040-69-7, Azasetron 123072-45-7, Aprosulate sodium
123122-54-3, Candoxatrilat 123122-55-4, Candoxatril 123258-84-4,
Itasetron 123308-22-5, Sezolamide 123407-36-3, Arteflene
123447-62-1, Prulifloxacin 123482-22-4, Zatosetron 123482-23-5,
Zatosetron maleate 123524-52-7, Azelnidipine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release
active ingredients)

IT 123618-00-8, Fedotozine 123774-72-1, Sargramostim 123830-79-5,
Teloxantrone hydrochloride 123948-87-8, Topotecan 124012-42-6,
Galocitabine 124423-84-3, Panadiplon 124436-59-5, Pirodavir
124439-07-2, Enadoline hydrochloride 124508-99-2, Sulfinosine
124770-85-0, Cyclobut A 124784-31-2, Erbulozole 124832-26-4,
Valaciclovir 124858-35-1, Nadifloxacin 124904-93-4, Ganirelix
124916-54-7, Celikalim 125251-66-3, Arbutamine hydrochloride
125279-79-0, Ersentilide 125472-02-8, Mivazerol 125533-88-2,
Mofarotene 125722-16-9, Enofelast 125926-17-2, Sarpogrelate
126062-18-8, Cyclobut G 126100-97-8, Dimiracetam 126297-39-0,
lissoclinamide 7 126443-96-7, Napavin 126544-47-6, Ciclesonide
126595-07-1, Propagermanium 126825-36-3, Bertosamil 127000-20-8,
Gadobenate dimeglumine 127045-41-4, Pazufloxacin 127294-70-6,
Balofloxacin 127304-28-3, Linarotene 127502-06-1, Tetrofosmin
127685-30-7, Seproxetine hydrochloride 127757-45-3, cyclic HPMPC
127757-91-9, Regramostim 127759-89-1, Lobucavir 127779-20-8,
Saquinavir 127785-64-2, Aureobasidin A 127943-53-7, Discodermolide
128075-79-6, Lufironil 128270-60-0, Bivalirudin 128312-51-6,
Cinalukast 128470-17-7, Sprodiamide 128505-88-4, Naphterpin
128768-09-2, Placetin A 129029-23-8, Ocaperidone 129038-42-2,
Echistatin 129242-14-4 129260-79-3, Loteprednol 129277-10-7,
Asperfuran 129369-64-8, Irtemazole 129388-07-4, Levdobutamine
lactobionate 129497-78-5, Verteporfin 129564-92-7, Azatoxin
129618-40-2, Nevirapine 129655-21-6, Bizelesin 129722-12-9,
Aripiprazole 129731-10-8, Vorozole 129938-20-1, Dapoxetine
hydrochloride 129981-36-8, Sampatrilat 130123-69-2, Faeriefungin
130167-69-0, Pegaspargase 130209-82-4, Latanoprost 130364-39-5,
Rubiginone B1 130370-60-4, Batimastat 130610-93-4, Niravoline
130641-36-0, Picumeterol 130641-38-2, Bindarit 130800-90-7,

Sipatrigine 130804-35-2, Lecimibide 130929-57-6, Entacapone
131069-91-5, Gadoversetamide 131081-40-8, Silteplase 131094-16-1,
Trafermin 131129-98-1, Mipragoside 131190-63-1, Saintopin
131410-48-5, Gadodiamide 131707-23-8, Arbidol 131741-08-7, Simendan
131956-33-7, Depsidomycin 131986-45-3, Xanomeline 132036-88-5,
Ramosetron 132073-72-4, Tetrazomine 132100-55-1, Dalvastatin
132199-13-4, Carsatrin succinate 132203-70-4, Cilnidipine 132210-43-6,
Cipamfylline 132236-18-1, Zifrosilone 132373-81-0, Vamicamide
132449-46-8, Lesopitron 132539-06-1, Olanzapine 132539-07-2,
Remifentanil hydrochloride 132722-74-8, Pirsidomine 133040-01-4,
Eprosartan 133099-04-4, Darifenacin 133247-60-6, Triflavin
133267-20-6, Artilide fumarate 133352-26-8, Cyclothiazomycin
133352-27-9, Lydicamycin 133432-71-0, Peldesine 133454-47-4,
Iloperidone 133692-55-4, Seprilose 133718-29-3, Revizinone
134088-74-7, Nartograstim 134143-28-5, Glaspimod 134208-18-7,
Mazapertine succinate 134308-13-7, Tolcapone 134352-59-3, Symakalim
134377-69-8, Safironil 134381-30-9, Conagenin 134499-06-2, Silipide
134523-03-8, Atorvastatin calcium 134523-84-5 134564-82-2, Befloxatone
134633-29-7, Tecogalan sodium 134678-17-4, Lamivudine 134861-62-4,
Dioxamycin 135003-30-4, Apadoline 135038-56-1, Glycopril
135038-57-2, Fasidotril 135202-79-8, Ilonidap 135247-46-0, Tylogenin
135257-45-3, crambescidin 816 135381-77-0, Flezelastine 135383-02-7,
Stipiamide 135459-90-4, Ranelic acid 135558-11-1, Lobaplatin
135819-69-1 135968-09-1, Lenograstim 136279-32-8, Teceleukin
136310-93-5, Tiotropium bromide 136381-85-6, Lintitript 136668-42-3,
Quiflapon 136777-43-0, Carvotroline hydrochloride 136816-75-6,
Atevirdine 136949-58-1, Iobitridol 137018-54-3, Okicenone
137023-81-5, Pannorin 137099-09-3, Turosteride 137109-71-8, Balazipone
137159-92-3, Aptiganel 137219-37-5, Dehydrodidemnin B 137234-62-9,
Voriconazole 137500-42-6, Darsidomine 137571-30-3 137647-92-8,
Axinastatin 1 137862-53-4, Valsartan 137893-48-2, Michellamine B
138071-82-6, Gadobutrol 138402-11-6, Irbesartan 138614-30-9, Icatibant
acetate 138660-96-5, Sevirumab 138705-61-0 138708-32-4, Ferpifosate
sodium 138742-43-5, Zankiren 138955-27-8 139110-80-8, Zanamivir
139133-26-9, Lexipafant 139225-22-2, Panamesine 139264-17-8,
Zolmitriptan 139403-31-9, Pimilprost 139481-59-7, Candesartan
139501-91-0, Hatomarubigin B 139501-92-1, Hatomarubigin C 139501-93-2,
Hatomarubigin D 139562-86-0, Hatomarubigin A 139664-68-9
139886-32-1, Milameline 140703-49-7, Meterelin 140703-51-1, Examorelin
140709-07-5 140932-79-2, Balhimycin 140945-32-0, Mapinastine
141205-31-4, Microcolin A 141410-98-2, Edobacomab 141505-33-1,
Levosimendan 141660-63-1, Iofratol 142298-00-8, Emoctakin
142439-86-9, Halomon 142632-32-4, Calanolide A 142864-19-5, Enlimomab
142880-36-2, Ilomastat 142985-55-5 143090-92-0, Anakinra
143248-63-9, Sinitrodil 143257-97-0, Sameridine 143257-98-1,
Lerisetron 143322-58-1, Eletriptan 143413-62-1, Betaclamycin B
143443-90-7, Ifetroban 143484-82-6, Azalanstat dihydrochloride
143486-90-2, Lurosetron mesylate 144285-84-7, ecteinascidin 722
144412-49-7, Lamifiban 144494-65-5, Tirofiban 144665-07-6, Lubeluzole
144701-48-4, Telmisartan 144849-63-8, Bisnafide 144916-42-7, Sonermin
145071-44-9, Itameline 145202-66-0, Rizatriptan benzoate 145216-43-9,
Forasartan 145414-12-6, Lirexapride 145599-86-6, Cerivastatin
145686-15-3, Azadirachtin E 145733-36-4, Tasosartan 146426-40-6,
Flavopiridol 146623-69-0, Saprisartan 146929-33-1, Cyclazosin
146939-27-7, Ziprasidone 147059-72-1, Trovafloxacin 147214-63-9,
Cyclothialidine 147221-93-0, Delavirdine mesylate 147249-33-0,
Aspalatone 147362-57-0, Loviride 147432-77-7, Ontazolast
147536-97-8, Bosentan 147541-45-5, Cilobradine 148317-76-4, Oracin
148504-51-2, Ripisartan 148611-75-0, Mirisetron maleate 148717-58-2,
Palauamine 148717-90-2, Squalamine 148937-32-0, Echicetin
149204-42-2, Kahalalide F 149260-80-0, Mycaperoxide B 149355-77-1,
Lamellarin-N triacetate 149488-17-5, Trovirdine 149633-91-0,
Leptolstatin 149649-22-9, Nafadotride 149715-96-8, spongistatin 1
149820-74-6, Xemilofiban 149845-07-8, Tiludronate disodium
149882-10-0, Lurtotecan 149904-87-0, Darglitazone sodium 149908-53-2,
Azimilide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release
active ingredients)

IT 150332-35-7, Pamaqueside 150378-17-9, Indinavir 150829-93-9, Nisamycin 150915-41-6, Perospirone 150977-36-9, Bromelain 151271-08-8, Imidazenil 151272-78-5, Antarelix 151319-34-5, Zaleplon 151581-23-6, Apaxifylline 151767-02-1, Montelukast sodium 152923-56-3, Dacliximab 152981-31-2, Inolimomab 153101-26-9, Regavirumab 153205-46-0, Asimadoline 153438-49-4, Dapitant 153723-34-3, Axinastatin 2 153723-35-4, Axinastatin 3 153858-68-5, Contortrostatin 154039-60-8, Marimastat 154212-56-3, Cosalane 154248-96-1, Iroplact 154277-21-1, Cypemycin 154361-50-9, Capecitabine 154397-77-0, Napsagatran 154612-39-2, Palinavir 155213-67-5, Ritonavir 155233-30-0, Curacin A 155319-91-8, Mangafodipir 155415-08-0, Inogatran 155660-91-6, Bistramide D 155660-92-7, Bistramide k 155773-56-1, Ferristene 155773-57-2, Pegorgotein 156039-69-9, Mixanpril 156250-43-0, Manumycin E 156317-47-4, Manumycin F 156586-89-9, Edrecolomab 156679-34-4, Lenercept 156712-35-5, Galdansetron hydrochloride 156769-21-0, Sanfetrinem 156790-85-1, Variolin B 157078-48-3, Isohomohalichondrin B 157207-83-5, bioxalomycin α-2 157857-21-1, Maspin 158792-24-6, Collismycin A 158792-25-7, Collismycin B 159445-63-3, Nateplase 159519-65-0, Pentafuside 161009-41-2 161600-01-7, MCC-555 162341-15-3, Darlucin A 163663-18-1, Protegrin 164325-97-7, Veroxanon 165101-51-9, Becaplermin 168482-36-8, cryptophycin 8 169494-85-3, Leptin 170861-63-9, JTT-501 171544-35-7, Ferumoxsil 172647-53-9, DRF-2189 172793-30-5 173046-02-1, Thiocoraline 173940-41-5, Tapgen 174305-65-8, Breflate 177402-92-5, Curiosin 178303-21-4, Ferucarbotran 178806-87-6, Eudragit RSPO 188364-40-1, CARN 700 189339-64-8 191034-25-0, L 168049 193012-35-0, FK614 196808-24-9, GW 1929 200139-38-4, Suradista 200631-89-6, CRE-16336 202532-75-0 207309-33-9, Motilide 209808-51-5, L 805645 212894-59-2, Pentrozole 213252-19-8, KRP-297 213411-84-8, BM-152054 213594-60-6, Balsalazide disodium 222834-30-2, Ragaglitazar) 245075-84-7, LR 90 246252-06-2, Gadolinium texaphyrin 250601-04-8, TAK559 251565-85-2 251572-86-8 308804-09-3, GW 9820 321942-74-9, Phensuccinal 324740-00-3, Vitaxin 331741-94-7, BMS298585 345631-66-5, Eveminomycin 385390-37-4, Pobilukast edamine 441772-39-0, Isobengazole 441772-43-6, Nagrestip 441772-66-3, Vinxaltine 441774-07-8, Spicamycin D 441774-77-2, Solverol 514172-76-0 516482-86-3, Sermorelin acetate 524675-01-2, CS 011 679809-58-6, Enoxaparin sodium 753015-01-9, Enterostatin 808103-38-0, Cepacidine 812697-78-2, CLX 0940 869997-64-8, R 483 873298-28-3, NIP 223 875140-52-6 875140-53-7 875338-33-3 875338-35-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel dosage form comprising modified-release and immediate-release active ingredients)

IT 60529-76-2, Thymopoietin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(receptor agonists; novel dosage form comprising modified-release and immediate-release active ingredients)

L27 ANSWER 2 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:55024 CAPLUS
DOCUMENT NUMBER: 142:134783
TITLE: 17-Acetamido-4-azasteroid derivatives as androgen receptor modulators for the treatment of related diseases
INVENTOR(S): Dankulich, William P.; Meissner, Robert S.; Mitchell, Helen J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005004807 | A2 | 20050120 | WO 2004-US20753 | 20040625 |
| WO 2005004807 | A3 | 20050407 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-483664P P 20030630
OTHER SOURCE(S): MARPAT 142:134783
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB 17-Acetamido-4-azasteroid derivs., I (X = H or halogen; R1 = H, CF3, CO, C1-3 alkyl, C1-4 alkoxy, halogen , hydroxymethyl, wherein said alkyl, and alkoxy are optionally substituted with 1-7 F atoms; Y = a substituted or unsubstituted hetercycle containing at least one nitrogen; R2, R3 = H, halogen, C1-8 alkyl, aminoalkyl, hydroxycarbonyl, CN, OH, etc.) were prepared as androgen receptor modulators for the treatment of related diseases. Thus, II was treated with Et3N, and iso-Bu chloroformate, followed by LiBH4 to give the alchol. This alc. was converted to the tosylate, which was converted to the nitrile. Oxidation of the nitrile resulted in formation of the corresponding acid which was treated with 2-oxopiperizine, EDC, and HOAt to give III.

IT Insulin-like growth factor-binding proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(IGFBP-3; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonist; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Anemia (disease)
(aplastic, treatment of; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Prostate gland, disease
(benign hyperplasia, treatment of; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Hyperplasia
(benign prostatic, treatment of; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(calcium, antagonist; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Mental and behavioral disorders
(depression, treatment of; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Prostaglandins
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(derivs.; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Bone, disease
(fracture, treatment of; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Lipids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hyperlipidemia, treatment of; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT Reproductive system, disease
(hypogonadism, treatment of; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)
IT Androgen receptors
Estrogen receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(modulators; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)
IT Bone, disease
(osteopenia, treatment of; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)
IT Drug delivery systems
Drug discovery
Human
(preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)
IT Bone morphogenetic proteins
Prostanoid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)
IT Antiestrogens
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)
IT Muscle
(sarcopenia, treatment of; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)
IT Menopause
(treatment of symptoms; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)
IT Alzheimer's disease
Arthritis
Atherosclerosis
Autoimmune disease
Bone, disease
**Cachexia**
Hematopoietic disorders
Hypercholesterolemia
Muscular dystrophy
Neoplasm
Obesity
Osteoporosis
Periodontium, disease
Prostate gland, neoplasm
Sexual disorders
Sleep apnea
(treatment of; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)
IT Transforming growth factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β-; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)
IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(γ, activator of; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)
IT 127464-60-2, Vascular endothelial growth factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonist; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)
IT 12001-79-5P, Vitamin k
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(derivs.; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)
IT 73984-05-1, BMP

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor of antagonism; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT 9028-35-7, HMG-CoA reductase 94716-09-3, Cathepsin K
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor of; preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT 9002-64-6, Parathyroid hormone 9002-72-6, Human growth hormone 9007-12-9, Calcitonin 61912-98-9, Insulin-like growth factor 67763-96-6, IGF I 67763-97-7, IGF II 106096-92-8, AFGF 106096-93-9, BFGF 192509-82-3, BMP 2 192509-86-7, BMP 3 193830-08-9, GDF5
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT 35212-22-7P, Ipriflavone 205944-50-9P, Osteoprotegerin 827039-75-8P 827039-76-9P 827039-77-0P 827039-78-1P 827039-79-2P 827039-80-5P 827039-81-6P 827039-82-7P 827039-83-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT 50-28-2, Estra-1,3,5(10)-triene-3,17-diol (17β)-, biological studies 53-16-7, Estrone, biological studies 64-96-0, U 11555A 67-96-9, Dihydrotachysterol 67-98-1, Mer 25 68-22-4, Norethindrone 71-58-9, Medroxyprogesterone acetate 471-34-1, Calcium carbonate, biological studies 911-45-5, **Clomiphene** 1406-16-2, Vitamin D 1845-11-0, Nafoxidene 2809-21-4 4717-38-8, 17β-Ethynyl estradiol 5863-35-4, CN 55945-27 7693-13-2, Calciumcitrate 10540-29-1, Tamoxifen 10596-23-3 15690-55-8, Zuclomiphene 15690-57-0, **Enclomiphene** 19356-17-3, 25-Hydroxy-vitamin D3 40391-99-9 41294-56-8 54573-75-0 56287-31-1, CI 680 66376-36-1, Alendronate 75330-75-5, Lovastatin 75755-07-6 78994-23-7, Levormeloxifene 79778-41-9, Neridronate 79902-63-9, Simvastatin 81093-37-0, Pravastatin 82413-20-5, Droloxifene 84449-90-1, Raloxifene 89778-26-7, Toremifene 89987-06-4, Tiludronate 93957-54-1, Fluvastatin 103909-75-7, 22-Oxacalcitriol 104121-92-8, ED 71 105462-24-6 114084-78-5, Ibandronate 116057-75-1, Idoxifene 118072-93-8, Zoledronate 121268-17-5, Alendronate monosodium trihydrate 121368-58-9, Olpadronate 130447-37-9, 19-Nor-1α,25 dihydroxyvitamin D3 131875-08-6, KH 1060 134404-52-7, EB 1089 134523-00-5, Atorvastatin 138330-18-4, Incadronate 141750-63-2, Nisvastatin 145599-86-6, Cerivastatin 147511-69-1, Pitavastatin 163659-89-0, 1α,25-Dihydroxy-16-ene-23-yne-vitamin D3 180064-38-4 180916-16-9, Lasofoxifene 182167-02-8, EM 652 182167-03-9, EM 800 198481-33-3, TSE 424 260055-05-8, Alendronate monosodium monohydrate 287714-41-4, Rosuvastatin 797050-81-8, U 100A (pharmaceutical)
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT 5625-67-2, Piperazinone 96692-02-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

IT 827039-84-9P 827039-85-0P 827039-86-1P 827039-87-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation 17-Acetamido-4-azasteroid derivs. as androgen receptor modulators and treatment of related diseases)

L27 ANSWER 3 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:995989 CAPLUS
DOCUMENT NUMBER: 142:747
TITLE: Combination treatment with strontium for the prophylaxis and/or treatment of cartilage and/or bone conditions
INVENTOR(S): Hansen, Christian; Nilsson, Henrik
PATENT ASSIGNEE(S): Nordic Bone A/S, Den.; Osteologix A/S; Christgau,

Stephan

SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004098618 | A2 | 20041118 | WO 2004-DK327 | 20040506 |
| WO 2004098618 | A3 | 20050324 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2524610 | AA | 20041118 | CA 2004-2524610 | 20040506 |
| EP 1622630 | A2 | 20060208 | EP 2004-731315 | 20040506 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| WO 2005108339 | A2 | 20051117 | WO 2005-DK307 | 20050505 |
| WO 2005108339 | A3 | 20051229 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |

| PRIORITY APPLN. INFO.: | | |
|---|---|---|
| DK 2003-691 | A | 20030507 |
| DK 2003-931 | A | 20030620 |
| DK 2003-1819 | A | 20031209 |
| US 2003-528548P | P | 20031209 |
| WO 2004-DK326 | A | 20040506 |
| WO 2004-DK327 | W | 20040506 |
| WO 2004-DK328 | A | 20040506 |
| DK 2004-1708 | A | 20041105 |

AB A combination treatment, wherein a strontium-containing compound together with one or more active substances capable of reducing the incidence of bone fracture and/or increasing bone d. and/or improving healing of fractured bone and/or improving bone quality are administered for use in the treatment and/or prophylaxis of cartilage and/or bone conditions.

IT Disease, animal
(Bechet's disease; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)

IT Bone, disease
(Paget's; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)

IT Drug interactions
(additive; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)

IT Development, mammalian postnatal
(adolescent; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)

IT Bone minerals
(bone mineral d. (BMD), bone mineral, d.; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone

conditions)
IT Pain
(bone; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Development, mammalian postnatal
(child; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Antirheumatic agents
Antitumor agents
Bone, disease
Bone resorption
Bone resorption inhibitors
Cartilage
Combination chemotherapy
Drug bioavailability
Drug delivery systems
Human
Hyperparathyroidism
**Myositis**
Neoplasm
Osteoarthritis
Osteomalacia
Osteoporosis
Pharmacokinetics
Prophylaxis
Rheumatoid arthritis
(combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Steroids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Glycosides
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coumarin; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Biological transport
(drug; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Intestine
(duodenum; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Bone, disease
(fracture; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Body weight
(gain; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Bone, disease
(hyperostosis; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Intestine
(jejunum; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Development, mammalian postnatal
(juvenile, osteoporosis; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Bone, neoplasm
(metastasis; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Antiarthritics
(osteoarthritis; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Bone, disease
(osteodystrophy; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Bone, disease
(osteolysis; combination treatment with strontium for prophylaxis

and/or treatment of cartilage and/or bone conditions)
IT Bone, disease
(osteopenia; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Bone, disease
(osteopetrosis; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Eye, disease
Osteoporosis
(osteoporosis-pseudoglioma syndrome; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Inflammation
Periodontium, disease
(periodontitis; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Intestine
(small; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Inflammation
Spinal column, disease
(spondylitis, Bechterew's disease; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Sulfonic acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(strontium salts; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Drug interactions
(synergistic; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT Drug delivery systems
(tablets, coated; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT 13598-36-2D, Phosphonic acid, alkylidenebis- derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Bisphosphonate; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT 182133-25-1, Arzoxifene
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(LY-353381; combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT 813-97-8P 868-19-9P 41839-80-9P 303730-87-2P 796104-86-4P 796842-36-9P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT 814-95-9 1633-05-2, Strontium carbonate 7759-02-6, Strontium sulfate 14332-40-2
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination treatment with strontium for prophylaxis and/or treatment of cartilage and/or bone conditions)
IT 50-14-6, Vitamin D2 56-53-1 67-97-0, Vitamin D3 67-98-1, Ethamoxytriphetol 446-72-0, Genistein 493-08-3D, Chroman, derivs. 526-26-1 553-39-9, Allenolic acid 569-57-3, Chlorotrianisene 592-89-2, Strontium formate 911-45-5, **Clomiphene** 1845-11-0, Nafoxidine 2188-25-2 2624-43-3, Cyclophenyl 2809-21-4 5630-53-5, Tibolone 5863-35-4, Nitromifene citrate 7440-24-6D, Strontium, salts 7446-28-8, Strontium phosphate 7783-48-4, Strontium fluoride 9002-64-6, Parathyroid hormone 10042-76-9, Strontium nitrate 10101-21-0 10476-81-0, Strontium bromide 10476-85-4, Strontium chloride 10476-86-5, Strontium iodide 10540-29-1, Tamoxifen 10596-23-3 13451-02-0, Strontium sulfite 13470-06-9, Strontium nitrite 13703-84-9, Strontium borate 16067-69-9 16088-89-4 18808-42-9

19657-12-6 23287-50-5 27540-07-4 29870-99-3 31477-60-8,
Ormeloxifene 34816-55-2, Moxestrol 40302-04-3 40391-99-9
40472-00-2 58429-84-8 60884-91-5 63524-05-0 66376-36-1,
Alendronate 68047-06-3, 4-Hydroxy-tamoxifen 71912-45-3 77599-17-8,
Panomifene 78994-23-7, Levormeloxifene 82413-20-5, Droloxifene
84449-90-1, Raloxifene 85169-08-0 86111-26-4, Zindoxifene
89778-26-7, Toremifene 89987-06-4, Tiludronate 98007-99-9
98774-23-3, Tesmilifene 103735-76-8, erythro-MEA 105462-24-6
114084-78-5, Ibandronate 115767-74-3, TAT-59 116057-68-2
116057-75-1, Idoxifene 118072-93-8, Zoledronate 124027-29-8
128607-22-7 129453-61-8, ICI 182780 129612-87-9, Miproxifene
135459-87-9, Strontium ranelate 165536-41-4, MDL-103323 180916-16-9,
Lasofoxifene 182167-03-9, EM-800 190791-29-8, CP-336156 198481-32-2,
Bazedoxifene 278172-05-7 452304-88-0 507471-56-9 796104-84-2
796104-90-0 796104-92-2 796104-97-7 796842-37-0 796842-38-1
796963-94-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(combination treatment with strontium for prophylaxis and/or treatment
of cartilage and/or bone conditions)

IT 10025-70-4P, Strontium chloride hexahydrate 120312-20-1P 127357-26-0P
796104-83-1P 796104-87-5P 796104-88-6P 796104-89-7P 796104-91-1P
796104-93-3P 796104-96-6P 796104-99-9P 796105-01-6P 796105-12-9P
796105-15-2P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(combination treatment with strontium for prophylaxis and/or treatment
of cartilage and/or bone conditions)

IT 7440-70-2, Calcium, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hypercalcemia; combination treatment with strontium for prophylaxis
and/or treatment of cartilage and/or bone conditions)

L27 ANSWER 4 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:722925 CAPLUS
DOCUMENT NUMBER: 141:218967
TITLE: Methods and compositions with **trans-clomiphene** for treating wasting and lipodystrophy
INVENTOR(S): Podolski, Joseph S.; Wiehle, Ronald
PATENT ASSIGNEE(S): Zonagen, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 12 pp., Cont.-in-part of U.S. Ser. No. 427,768.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2004171697 | A1 | 20040902 | US 2003-712546 | 20031112 |
| WO 2003005954 | A2 | 20030123 | WO 2002-US21524 | 20020709 |
| WO 2003005954 | A3 | 20031023 | | |
| WO 2003005954 | B1 | 20031204 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| US 2004097597 | A1 | 20040520 | US 2003-427768 | 20030430 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 2001-304313P | P | 20010709 |
| WO 2002-US21524 | A2 | 20020709 |
| US 2003-427768 | A2 | 20030430 |

AB The invention discloses compns. and methods useful for treating wasting, especially a loss of muscle mass. The present invention also discloses compns. and methods useful for treating lipodystrophy. The compns. and methods of the present invention are particularly beneficial to **HIV** -infected individuals.

IT Immunostimulants
(adjuvants; methods and compns. with **trans-clomiphene** for treating wasting and lipodystrophy)

IT Drug delivery systems
(carriers; methods and compns. with **trans-clomiphene** for treating wasting and lipodystrophy)

IT **AIDS** (disease)
Blood serum
Body weight
Bone
CD4-positive T cell
Combination chemotherapy
Erythrocyte
Human
Human immunodeficiency virus
Kidney
Lipodystrophy
Liver
Lymphocyte
Osteoblast
Platelet (blood)
(methods and compns. with **trans-clomiphene** for treating wasting and lipodystrophy)

IT Hemoglobins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(methods and compns. with **trans-clomiphene** for treating wasting and lipodystrophy)

IT Antiestrogens
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. with **trans-clomiphene** for treating wasting and lipodystrophy)

IT Muscle
(modulating mass of; methods and compns. with **trans-clomiphene** for treating wasting and lipodystrophy)

IT Disease, animal
(wasting; methods and compns. with **trans-clomiphene** for treating wasting and lipodystrophy)

IT 50-99-7, D-Glucose, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(blood; methods and compns. with **trans-clomiphene** for treating wasting and lipodystrophy)

IT 57-88-5, Cholesterol, biological studies 58-22-0, Testosterone 60-27-5, Creatinine 7440-23-5, Sodium, biological studies 9000-86-6, ALT 9001-78-9, Alkaline phosphatase 9002-62-4, Prolactin, biological studies 9002-67-9, LH 9002-68-0, FSH
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(methods and compns. with **trans-clomiphene** for treating wasting and lipodystrophy)

IT 50-41-9, **Clomid** 15690-55-8, cis-**Clomiphene** 15690-57-0, **trans-Clomiphene**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. with **trans-clomiphene** for treating wasting and lipodystrophy)

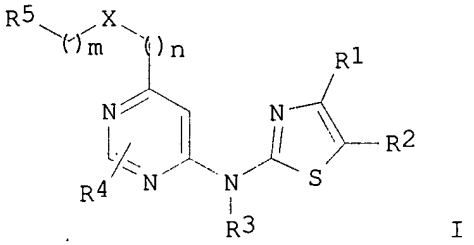
L27 ANSWER 5 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:412750 CAPLUS
DOCUMENT NUMBER: 140:423687
TITLE: Preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors
INVENTOR(S): Hartman, George D.; Hoffman, Jacob M.; Smith, Anthony M.; Tucker, Thomas J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004041164 | A2 | 20040521 | WO 2003-US34100 | 20031024 |
| WO 2004041164 | A3 | 20041007 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2503715 | AA | 20040521 | CA 2003-2503715 | 20031024 |
| EP 1558609 | A2 | 20050803 | EP 2003-779322 | 20031024 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |

PRIORITY APPLN. INFO.: US 2002-422313P P 20021030
WO 2003-US34100 W 20031024

OTHER SOURCE(S): MARPAT 140:423687
GI



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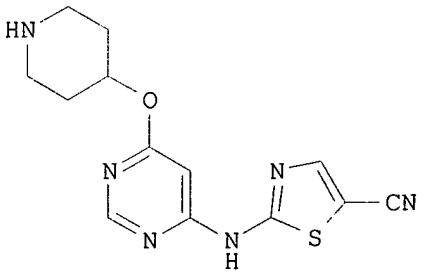

II

AB Title compds. I [X = O, S, amino; m,n = 0-3; R1-2, R4 = H, OH, alkoxy, CN, etc.; R3 = H, sulfonyl, acyl, carboxy, etc.; R5 = heterocyclyl] are prepared For instance, tert-Bu 4-[(6-aminopyrimidin-4-yl)oxy]piperidine-1-carboxylate (preparation given) is reacted with 2-chlorothiazole-5-carbonitrile (THF, NaH) and the resulting product deprotected (CH2Cl2, TFA) to give II. I inhibit, regulate and/or modulate kinase signal transduction; they are useful in the treatment of kinase-dependent diseases and conditions, such as angiogenesis, cancer, tumor growth, atherosclerosis, age related macular degeneration, retinal ischemia, macular edema, diabetic

retinopathy and inflammatory diseases.

IT Troponins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(I, combination pharmaceutical; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Lung, neoplasm
(adenocarcinoma; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Meningitis
(bacterial, tissue damage from, treatment; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Mammary gland, neoplasm
(carcinoma; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Intestine, neoplasm
(colorectal; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Antihypertensives
Antitumor agents
Cytotoxic agents
(combination pharmaceutical; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Gonadotropins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Photodynamic therapy
(combination therapy; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Dermatitis
(contact; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Allergy
(delayed hypersensitivity; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Eye, disease
(diabetic retinopathy; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Uterus, disease
(endometriosis; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Growth factors, animal
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fibroblast-derived growth factors, inhibitor, combination pharmaceutical; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Neuroglia, neoplasm
(glioblastoma; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Lymphoma
(histiocytic; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Ovary, disease
(hyperstimulation syndrome; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Integrins
Interleukin 12
Platelet-derived growth factors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor, combination pharmaceutical; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Eye, disease
(macula, senile degeneration; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Carcinoma
(mammary; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Androgen receptors
Estrogen receptors
Retinoid receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(modulator, combination pharmaceutical; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Angiogenesis inhibitors
Anti-inflammatory agents
Antiarthritics
Bone, disease
Eye, disease
Human
Larynx, neoplasm
Leukemia
Lung, neoplasm
Neoplasm
Pancreas, neoplasm
Preeclampsia
Psoriasis
Rickets
Stomach, neoplasm
(preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Carcinoma
(pulmonary adenocarcinoma; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Carcinoma
(pulmonary small-cell; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Lung, neoplasm
(small-cell carcinoma; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Interferons
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α, inhibitor, combination pharmaceutical; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Integrins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(αIIbβ3, antagonist, combination pharmaceutical; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT Peroxisome proliferator-activated receptors
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(γ, agonist, combination pharmaceutical; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT 127464-60-2, Vascular endothelial growth factor
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibody to, combination pharmaceutical; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT 50-35-1, Thalidomide 911-45-5, **Clomifene** 9002-67-9, Luteinizing hormone 9002-68-0, Follicle stimulating hormone 10540-29-1, Tamoxifen 25614-03-3, Bromocriptine 33069-62-4, Paclitaxel 37300-21-3, Pentosan polysulfate 84449-90-1, Raloxifene 86090-08-6, Angiostatin 99519-84-3, Carboxyamidotriazole 110942-08-0, Luprolide 117048-59-6, Combretastatin A-4 144494-65-5, Tirofiban 148717-90-2, Squalamine 180288-69-1, Trastuzumab 561321-04-8, 6-(O-Chloroacetylcarbonyl)fumagillol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT 9028-35-7, HMG-CoA reductase 9068-38-6, Reverse transcriptase 39391-18-9, Cyclooxygenase 131384-38-8, Prenylprotein transferase 141907-41-7, Matrix metalloproteinase 144114-21-6, **HIV** protease 329900-75-6, COX-2
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(inhibitor, combination pharmaceutical; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT 150428-23-2, Cyclin-dependent kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT 436852-23-2P, 2-[(6-Chloro-2-methylpyrimidin-4-yl)amino]-1,3-thiazole-5-carbonitrile 691400-75-6P, tert-Butyl 4-[[6-[(5-cyano-1,3-thiazol-2-yl)amino]pyrimidin-4-yl]oxy]piperidine-1-carboxylate 691400-79-0P, tert-Butyl 4-[[6-[(5-phenyl-1,3-thiazol-2-yl)amino]pyrimidin-4-yl]oxy]piperidine-1-carboxylate 691400-82-5P 691400-85-8P, tert-Butyl 4-[[[6-[(5-phenyl-1,3-thiazol-2-yl)amino]pyrimidin-4-yl]oxy]methyl]piperidine-1-carboxylate 691400-91-6P, 2-[[2-Methyl-6-(piperidin-4-yloxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691400-99-4P, 2-[[2-Methyl-6-(piperidin-4-ylmethoxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691401-00-0P 691401-17-9P, tert-Butyl [4-[[[6-[(5-cyano-1,3-thiazol-2-yl)amino]-2-methylpyrimidin-4-yl]oxy]methyl]piperidin-1-yl]acetate 691401-18-0P, [4-[[[6-[(5-Cyano-1,3-thiazol-2-yl)amino]-2-methylpyrimidin-4-yl]oxy]methyl]piperidin-1-yl]acetic acid 691401-45-3P, tert-Butyl 4-[[6-[(5-cyanothiazol-2-yl)amino]-2-methylpyrimidin-4-yl]amino]piperidine-1-carboxylate 691401-48-6P, tert-Butyl 4-[[6-[[(5-cyano-1,3-thiazol-2-yl)amino]methyl]-2-methylpyrimidin-4-yl]amino]piperidine-1-carboxylate
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT 691400-77-8P, 2-[[6-(Piperidin-4-yloxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691400-78-9P, 2-[[6-(Piperidin-4-yloxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691400-80-3P, N-(5-Phenyl-1,3-thiazol-2-yl)-6-(piperidin-4-yloxy)pyrimidin-4-amine 691400-81-4P, N-(5-Phenyl-1,3-thiazol-2-yl)-6-(piperidin-4-yloxy)pyrimidin-4-amine trifluoroacetate 691400-83-6P, 2-[[6-(Piperidin-4-ylmethoxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691400-84-7P, 2-[[6-(Piperidin-4-ylmethoxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691400-86-9P, N-(5-Phenyl-1,3-thiazol-2-yl)-6-(piperidin-4-ylmethoxy)pyrimidin-4-amine 691400-87-0P, N-(5-Phenyl-1,3-thiazol-2-yl)-6-(piperidin-4-ylmethoxy)pyrimidin-4-amine trifluoroacetate 691400-90-5P, 2-[[2-Methyl-6-(piperidin-4-yloxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691400-92-7P, N-(5-Phenyl-1,3-thiazol-2-yl)-6-(piperidin-4-yloxy)-2-methylpyrimidin-4-amine 691400-93-8P 691400-94-9P, 2-[[2-Methyl-6-((3R)-pyrrolidin-3-yloxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691400-95-0P, 2-[[2-Methyl-6-((3R)-pyrrolidin-3-yloxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691400-96-1P, 2-[[2-Methyl-6-((3S)-pyrrolidin-3-yloxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691400-97-2P, 2-[[2-Methyl-6-((3S)-pyrrolidin-3-yloxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691400-98-3P, 2-[[2-Methyl-6-(piperidin-4-ylmethoxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-01-1P, 2-[[2-Methyl-6-(morpholin-2-ylmethoxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-02-2P, 2-[[2-Methyl-6-(morpholin-2-ylmethoxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691401-03-3P, 2-[[2-Methyl-6-(tetrahydro-2-pyran-4-yloxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-04-4P, 2-[[2-Methyl-6-(tetrahydro-2-pyran-4-yloxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691401-05-5P, 2-[[2-Isopropyl-6-(piperidin-4-yloxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-06-6P, 2-[[2-Isopropyl-6-(piperidin-4-yloxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691401-11-3P, 2-[[2-Methyl-6-[[1-(2-(morpholin-4-yl)ethyl)piperidin-4-yl]oxy]pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-15-7P, 2-[4-[[6-[(5-Cyano-1,3-thiazol-2-yl)amino]-2-methylpyrimidin-4-yl]oxy]piperidin-1-yl]-N-isopropylacetamide 691401-16-8P 691401-19-1P, N-(tert-Butyl)-2-[4-[[[6-[(5-cyano-1,3-thiazol-2-yl)amino]-2-methylpyrimidin-4-yl]oxy]methyl]piperidin-1-yl]acetamide 691401-20-4P, 2-[[2-Methyl-6-(3-(morpholin-4-yl)propoxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-21-5P, 2-[[2-Methyl-6-(3-(morpholin-4-yl)propoxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile

trifluoroacetate 691401-22-6P, 2-[[2-Methyl-6-(2-(morpholin-4-yl)ethoxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-23-7P, 2-[[2-Methyl-6-(2-(morpholin-4-yl)ethoxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691401-24-8P, 2-[[2-Methyl-6-(2-(piperidin-1-yl)ethoxy)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-25-9P 691401-26-0P, 2-[[2-Methyl-6-[(2-(morpholin-4-yl)ethyl)amino]pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-27-1P, 2-[[2-Methyl-6-[(2-(morpholin-4-yl)ethyl)amino]pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691401-29-3P, 2-[[6-[(3-(Morpholin-4-yl)propyl)amino]pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-30-6P, 2-[[6-[(3-(Morpholin-4-yl)propyl)amino]pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691401-31-7P, 2-[[2-Methyl-6-(tetrahydro-2H-pyran-4-ylamino)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-32-8P, 2-[[6-[[3-(1H-Imidazol-1-yl)propyl]amino]-2-methylpyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-33-9P 691401-34-0P 691401-35-1P, 2-[[6-[(1,4-Dioxan-2-ylmethyl)amino]-2-methylpyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-36-2P, 2-[[6-[((1,4-Dioxan-2-yl)methyl)amino]-2-methylpyrimidin-4-yl]amino]thiazole-5-carbonitrile trifluoroacetate 691401-37-3P 691401-38-4P 691401-40-8P, 2-[[2-Methyl-6-(tetrahydrofuran-3-ylamino)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-41-9P, 2-[[2-Methyl-6-(tetrahydrofuran-3-ylamino)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691401-44-2P, 2-[4-[[6-[(5-Cyanothiazol-2-yl)amino]-2-methylpyrimidin-4-yl]amino]piperidin-1-yl]-N-isopropylacetamide trifluoroacetate 691401-46-4P, 2-[[2-Methyl-6-(piperidin-4-ylamino)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-47-5P, 2-[[2-Methyl-6-(piperidin-4-ylamino)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691401-49-7P, 2-[[2-Methyl-6-[(piperidin-4-ylmethyl)amino]pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-50-0P, 2-[[2-Methyl-6-[(piperidin-4-ylmethyl)amino]pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691401-52-2P, 2-[[5-Methyl-6-(piperidin-4-ylamino)pyrimidin-4-yl]oxy]-1,3-thiazole-5-carbonitrile 691401-53-3P, 2-[[5-Methyl-6-(piperidin-4-ylamino)pyrimidin-4-yl]oxy]-1,3-thiazole-5-carbonitrile trifluoroacetate 691401-55-5P, 2-[[2-Methyl-6-[(2-(morpholin-4-yl)ethyl)thio]pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-59-9P, 2-[[6-(Piperidin-4-ylthio)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile 691401-60-2P, 2-[[6-(Piperidin-4-ylthio)pyrimidin-4-yl]amino]-1,3-thiazole-5-carbonitrile trifluoroacetate 691401-61-3P, 2-[4-[[6-((5-Cyanothiazol-2-yl)amino)-2-methylpyrimidin-4-yl]amino]piperidin-1-yl]-N-isopropylacetamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT 75-31-0, Isopropylamine, reactions 75-64-9, tert-Butylamine, reactions 123-00-2, 3-(Morpholin-4-yl)propan-1-amine 622-40-2, 2-(Morpholin-4-yl)ethanol 767-16-8, 6-Amino-2-methylpyrimidin-4-ol 1193-22-2, 4-Hydroxy-6-aminopyrimidine 1749-68-4, 6-Chloro-2-methylpyrimidin-4-amine 1850-98-2, 2-Isopropyl-4,6-dichloropyrimidine 2038-03-1, 4-(2-Aminoethyl)morpholine 2081-44-9, Tetrahydro-2H-pyran-4-ol 3040-44-6, 2-Piperidin-1-ylethanol 3647-69-6, 4-(2-Chloroethyl)morpholine hydrochloride 5036-48-6, 3-(1H-Imidazol-1-yl)propan-1-amine 5292-43-3, tert-Butyl bromoacetate 6338-70-1 20120-24-5, Ethyl 3-(morpholin-4-yl)propanoate 38041-19-9, Tetrahydro-2H-pyran-4-amine 45697-13-0 51640-36-9, 2-Chloro-1,3-thiazole-5-carbonitrile 73874-95-0, tert-Butyl piperidin-4-ylcarbamate 75726-96-4, 2-Bromo-N-isopropylacetamide 87120-72-7, tert-Butyl 4-aminopiperidine-1-carboxylate 101469-92-5, tert-Butyl (S)-3-hydroxypyrrolidine-1-carboxylate 109384-19-2, tert-Butyl 4-hydroxypiperidine-1-carboxylate 109431-87-0, tert-Butyl (R)-3-hydroxypyrrolidine-1-carboxylate 123855-51-6, tert-Butyl 4-(hydroxymethyl)piperidine-1-carboxylate 144222-22-0, tert-Butyl 4-aminomethylpiperidine-1-carboxylate 154917-45-0, 1,4-Dioxan-2-ylmethylamine 189321-66-2, 4-(tert-Butoxycarbonyl)morpholine-2-carboxylic acid 204512-94-7, Tetrahydrofuran-3-amine hydrochloride 329794-40-3, 2-Chloro-5-phenyl-1,3-thiazole 436851-99-9, 2-[(6-Chloropyrimidin-4-yl)amino]-1,3-thiazole-5-carbonitrile

436852-24-3, 2-[(6-Chloro-5-methylpyrimidin-4-yl)amino]-1,3-thiazole-5-carbonitrile 691401-39-5, 2-[(6-Methoxy-2-methylpyrimidin-4-yl)amino]-1,3-thiazole-5-carbonitrile 691401-58-8, tert-Butyl 4-[(6-aminopyrimidin-4-yl)thio]piperidine-1-carboxylate
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT 4441-30-9P, 3-(Morpholin-4-yl)propan-1-ol 89280-06-8P, 6-Amino-2-methylpyrimidine-4-thiol 691400-74-5P, tert-Butyl 4-[(6-aminopyrimidin-4-yl)oxy]piperidine-1-carboxylate 691400-88-1P, tert-Butyl 4-[(6-amino-2-methylpyrimidin-4-yl)oxy]piperidine-1-carboxylate 691400-89-2P, tert-Butyl 4-[[6-[(5-cyano-1,3-thiazol-2-yl)amino]-2-methylpyrimidin-4-yl]oxy]piperidine-1-carboxylate 691401-07-7P, 6-Chloro-2-isopropylpyrimidin-4-amine 691401-09-9P 691401-10-2P, 2-Methyl-6-[[1-(2-(morpholin-4-yl)ethyl)piperidin-4-yl]oxy]pyrimidin-4-amine 691401-12-4P, tert-Butyl [4-[[6-[(5-cyano-1,3-thiazol-2-yl)amino]-2-methylpyrimidin-4-yl]oxy]piperidin-1-yl]acetate 691401-14-6P, [4-[[6-[(5-Cyano-1,3-thiazol-2-yl)amino]-2-methylpyrimidin-4-yl]oxy]piperidin-1-yl]acetic acid trifluoroacetate 691401-42-0P, tert-Butyl [1-[2-(isopropylamino)-2-oxoethyl]piperidin-4-yl]carbamate 691401-51-1P 691401-54-4P, 2-Methyl-6-[(2-(morpholin-4-yl)ethyl)thio]pyrimidin-4-amine 691401-56-6P, tert-Butyl 4-[(6-amino-2-methylpyrimidin-4-yl)thio]piperidine-1-carboxylate 691401-57-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

IT 80449-02-1, Tyrosine kinase
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(related disease, prevention/treatment; preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors)

L27 ANSWER 6 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:521462 CAPLUS
DOCUMENT NUMBER: 137:88442
TITLE: Incensole and furanogermacrens and compounds in treatment for inhibiting neoplastic lesions and microorganisms
INVENTOR(S): Shanahan-Pendergast, Elisabeth
PATENT ASSIGNEE(S): Ire.
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 2002053138 | A2 | 20020711 | WO 2002-IE1 | | 20020102 |
| WO 2002053138 | A3 | 20020919 | | | |
| W: AE, AG, AT, AU, BB, BG, CA, CH, CN, CO, CU, CZ, LU, LV, MA, MD, UA, UG, US, VN, YU, RU, TJ, TM | | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, AT, BE, CH, CY, DE, ES, FI, ML, MR, NE, SN, TD, TG | | | | | |
| EP 1351678 | A2 | 20031015 | EP 2002-727007 | | 20020102 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | | |
| US 2004092583 | A1 | 20040513 | US 2004-250535 | | 20040102 |
| PRIORITY APPLN. INFO.: | | | IE 2001-2 | A | 20010102 |
| | | | WO 2002-IE1 | W | 20020102 |

OTHER SOURCE(S): MARPAT 137:88442

AB The invention discloses the use of incensole and/or furanogermacrens, derivs. metabolites and precursors thereof in the treatment of neoplasia, particularly resistant neoplasia and immunodysregulatory disorders. These compds. can be administered alone or in combination with conventional chemotherapeutic, antiviral, antiparasite agents, radiation and/or surgery. Incensole and furanogermacren and their mixture showed antitumor activity against various human carcinomas and melanomas and antimicrobial

activity against Staphylococcus aureus and Enterococcus faecalis.

IT Proteins
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A, immunomodulator based on, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Leukemia
Lymphoma
(B-cell; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Fusion proteins (chimeric proteins)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(BCR-ABL, antagonists, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Inflammation
(Crohn's disease, treatment of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Intestine, disease
(Crohn's, treatment of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Canarypox virus
(IL-2 of, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT GTPase-activating protein
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(RasGAP, inhibitors, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Sdi 1, mimetics, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Skin, neoplasm
(Sezary syndrome; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Leukemia
Lymphoma
(T-cell; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Transcription factors
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(WT1 (Wilms' tumor suppressor 1), therapy based on; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Keratosis
(actinic; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Leukemia
(acute; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Lung, neoplasm
(adenocarcinoma; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Melanoma
(amelanotic; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Urokinase-type plasminogen activator receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-dorsalizing morphogenetic protein-1, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as

antitumor and antimicrobial agents)
IT Antitumor agents
(antineoplastons, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Nutrients
(antinutrients, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Drug resistance
(antitumor; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Lung, disease
(aspergillosis, treatment of immunodysregulation condition caused by; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Infection
(bacterial, intracellular or extracellular, treatment of immunodysregulation condition caused by; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(c-Raf, antagonists, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Mycosis
(candidiasis, treatment of immunodysregulation condition caused by; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Prostate gland, neoplasm
(carcinoma, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Ovary, neoplasm
Stomach, neoplasm
(carcinoma; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Mycobacterium
(cell wall sk and monophosphoryl lipid A, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Diterpenes
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cembranoid, alcs.; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Diterpenes
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cembranoid; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Uterus, disease
(cervix, dysplasia; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Uterus, neoplasm
(cervix; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Porphyrins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chlorins, benzo-, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Porphyrins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chlorins, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Leukemia
(chronic; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-, enteric coating of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Intestine, neoplasm
(colon, carcinoma; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Intestine, neoplasm
(colon, polyp; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Intestine
(colon, precancerous lesion in; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Carcinoma
Intestine, neoplasm
(colon; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Polyoxyalkylenes, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates with pyridoxylated Hb; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Quinones
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclopentanthraquinones, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Immunity
(disorder, treatment of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Stem cell
(division inhibitors, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Carbohydrates, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug delivery systems containing; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Antibodies and Immunoglobulins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug targeting to **HIV** infected cells using; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Tumor antigens
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(drug targeting with monoclonal antibody to; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Bronchi, disease
Prostate gland, disease
(dysplasia; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Skin, neoplasm
(dysplastic nevus syndrome; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Dendritic cell
(enhancement of endogenous precursor; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Heat-shock proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(enhancement of endogenous; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enteric coating of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Drug delivery systems
(enteric-coated; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Drug delivery systems

(enteric; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Escherichia coli
(enterohemorrhagic, treatment of immunodysregulation condition caused by infection with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Escherichia coli
(enteroinvasive, treatment of immunodysregulation condition caused by infection with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Escherichia coli
(enteropathogenic, treatment of immunodysregulation condition caused by infection with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Escherichia coli
(enterotoxigenic, treatment of immunodysregulation condition caused by infection with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Lung, neoplasm
(epidermoid; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Gene therapy
(erythrocyte, vector system, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(for apoptosis, modulators of, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Carcinoma
(gastric; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Multidrug resistance
(gene inhibitor, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Apoptosis
(gene modulators or regulators, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Erythrocyte
(gene therapy vector system, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Envelope proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gp120env, drug targeting to **HIV** infected cells using antibodies to; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Envelope proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gp160env, drug targeting to **HIV** infected cells using antibodies to; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Leukemia
(hairy-cell; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Peptides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunostimulant, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Chemotherapy
Parasiticides
Radiotherapy
Surgery
(in combination with; incensole and furanogermacrens and compds. as

antitumor and antimicrobial agents)
IT Adrenal gland, neoplasm
Anti-**AIDS** agents
Anti-infective agents
Antiarthritics
Antiasthmatics
Antidiabetic agents
Antidiarrheals
Antitumor agents
Bladder, neoplasm
Brain, neoplasm
Burn
Central nervous system, neoplasm
Drug delivery systems
Enterococcus faecalis
Hematopoietic neoplasm
Hodgkin's disease
Human
Lymphoma
Mammary gland, neoplasm
Melanoma
Mouth, neoplasm
Multiple myeloma
Neoplasm
Newborn
Ovary, neoplasm
Pancreas, neoplasm
Prostate gland, neoplasm
Sarcoma
Staphylococcus aureus
Stomach, neoplasm
Testis, neoplasm
(incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Polyoxyalkylenes, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Yeast
(infection with, treatment of immunodysregulation condition caused by; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Intestine, disease
(inflammatory, treatment of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Cartilage
(inhibitor derived from, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Stem cell
(inhibitor, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Insulin-like growth factor I receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Translation, genetic
(inhibitors of, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Signal transduction, biological
(inhibitors or modulators, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Macrophage migration inhibitory factor
Ras proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Insulin-like growth factor-binding proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(insulin-like growth factor I-binding, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Parasite
(intracellular or extracellular infection with, treatment of immunodysregulation condition caused by; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Gamma ray
(irradiation, treatment of immunodysregulation condition caused by treatment with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Intestine, disease
(irritable bowel syndrome, treatment of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Digestive tract
(irritation, treatment of immunodysregulation condition caused by; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Paracoccidioides
(juvenile paracoccidiomyosis, treatment of immunodysregulation condition caused by; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Lung, neoplasm
(large-cell carcinoma; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Bladder, disease
Skin, disease
(lesions; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Virus
(lipid envelope, treatment of immunodysregulation condition caused by infection with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Peptides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipophilic disaccharide, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Drug delivery systems
(liposomes; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Peptides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lytic, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Pulverization
(micronization; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Double stranded RNA
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mismatched, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal, conjugates, with liposome or carbohydrate vehicles, to tumor-associated antigen; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal, to human chorionic gonadotropin, pharmaceutical formulation further including; incensole and furanogermacrens and

compds. as antitumor and antimicrobial agents)
IT Leukemia
(monocytic; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Lipid A
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monophosphates, and mycobacterium cell wall sk, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Nerve, disease
(motor, treatment of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Firmicutes
(multi-drug resistant; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Gene
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(multidrug resistance, inhibitor, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Leukemia
(myelogenous; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Leukemia
(myelomonocytic; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Drug delivery systems
(nasal; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Nerve, neoplasm
(neuroblastoma; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Antioxidants
(nitroxide, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Lymphocyte
(null cell, leukemia; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Interleukin 2
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(of canarypox virus, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Cytokines
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(oral inducer, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Drug delivery systems
(oral; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Carcinoma
(ovarian; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Drug delivery systems
(parenterals; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Antiviral agents
(pharmaceutical formulation further containing; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical formulation further containing; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Angiogenesis inhibitors
Antivenoms
Cytotoxic agents

Immunostimulants
Mycobacterium bovis
Venoms
(pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Antiandrogens
Antiestrogens
Antisense oligonucleotides
Estrogens
Hormones, animal, biological studies
Interleukins
Leukemia inhibitory factor
Neuregulin 1
Oligonucleotides
Polyamines
Ribozymes
Steroids, biological studies
Taxanes
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Disease, animal
(polyposis syndrome; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Fatty acids, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(poppy seed-oil, Et esters, labeled with iodine-131, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Central nervous system, disease
Kidney, disease
Lung, disease
Mammary gland, disease
Stomach, disease
(precancerous lesion in; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Drug delivery systems
(prodrugs; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Carcinoma
(prostatic, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Carcinoma
(pulmonary adenocarcinoma; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Carcinoma
(pulmonary large-cell; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Carcinoma
(pulmonary small-cell; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Hemoglobins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reaction products, with pyridoxal phosphate, conjugates with polyoxyethylene, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Drug delivery systems
(rectal; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Kidney, neoplasm
(renal cell carcinoma; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Carcinoma
(renal cell; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Antitumor agents
(resistance to; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(saporin, fibroblast growth factor conjugates; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(senescence-derived inhibitor 1, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Oligonucleotides
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sense, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Shock (circulatory collapse)
(septic, treatment of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Proteins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(single chain antigen binding protein, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Cell wall
(sk of mycobacteria and monophosphoryl lipid A, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Leukemia
(small cell; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Lung, neoplasm
(small-cell carcinoma; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Neoplasm
(solid; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Carcinoma
(squamous cell; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Drug delivery systems
(sublingual; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Glycosaminoglycans, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthetic, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Lupus erythematosus
(systemic, treatment of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Human immunodeficiency virus
(targeting to cells infected with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(thymopoietin, agonists, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Drug delivery systems
(topical; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)
IT Stem cell factor
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(totipotent, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Adeno-associated virus
Balantidium
Balantidium coli
Borrelia
Campylobacter
Candida
Coronavirus
Cryptococcus (fungus)
Cryptosporidium
DNA viruses
Entamoeba
Entamoeba histolytica
Filovirus
Flavivirus
Haemophilus
Hantavirus
Human papillomavirus
Human parainfluenza virus
Human poliovirus
Influenza virus
Legionella
Leishmania
Leishmania braziliensis
Leishmania donovani
Leishmania mexicana
Leishmania tropica
Listeria
Measles virus
Mycoplasma
Papillomavirus
Pestivirus
Picornaviridae
Plasmodium berghei
Plasmodium falciparum
Plasmodium malariae
Plasmodium ovale
Plasmodium vivax
Pneumocystis
Pneumocystis carinii
Poxviridae
Pseudomonas
RNA viruses
Respiratory syncytial virus
Retroviridae
Rhinovirus
Rubivirus
Salmonella
Shigella
Staphylococcus
Streptococcus
Togaviridae
Toxoplasma
Toxoplasma gondii
Trichomonas
Trichomonas vaginalis
Trypanosoma
Trypanosoma brucei
Trypanosoma cruzi
Trypanosoma gambiense
Trypanosoma rhodesiense
Vibrio
Yersinia
(treatment of immunodysregulation condition caused by infection with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Corticosteroids, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)

(treatment of immunodysregulation condition caused by treatment with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Nucleoside analogs
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of immunodysregulation condition caused by treatment with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Immunosuppressants
Mycosis
Protozoa
Wound
(treatment of immunodysregulation condition caused by; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Arthritis
Asthma
Autoimmune disease
**Cachexia**
Cirrhosis
Diabetes mellitus
Diarrhea
Multiple sclerosis
Respiratory distress syndrome
(treatment of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Cytotoxic agents
(tyrphostins, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Drug delivery systems
(vaginal; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Infection
(viral, treatment of immunodysregulation condition caused by; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Disease, animal
(wasting, treatment of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α, n1, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α, n3, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α-2a, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α-2b, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Lactams
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β-, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Interferons

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β1, a, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT Interferons
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(γ, 1b, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 37221-79-7, Vasoactive intestinal peptide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antagonist, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 9002-06-6, Thymidine kinase
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antagonists, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 505-60-2, Mustard
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anticancer, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 7585-39-9, β-Cyclodextrin 7585-39-9D, β-Cyclodextrin, hydroxypropyl derivs. 10016-20-3, α-Cyclodextrin 12619-70-4, Cyclodextrin 17465-86-0, γ-Cyclodextrin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as pharmaceutical carrier; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 80-62-6, Methyl methacrylate 2867-47-2, (2-Dimethylaminoethyl) methacrylate 9004-38-0, Cellulose acetate phthalate 34346-01-5, Poly(lactic acid-glycolic acid) 441015-98-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enteric coating of; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 121749-39-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(epharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 54-47-7D, Pyridoxal phosphate, reaction products with Hb conjugates 76-49-3, Bornyl acetate 80-57-9, Verbenone 87-44-5, β-Caryophyllene 88-84-6, β-Guaiene 99-49-0, Carvone 99-83-2, α-Phellandrene 99-87-6, p-Cymene 112-14-1, Octyl acetate 123-35-3, Myrcene 473-11-0, Eudesmane 489-80-5, Guaiane 495-61-4, β-Bisabolene 502-61-4, Farnesene 507-70-0, Borneol 511-59-1, β-Santalene 512-61-8, α-Santalene 515-12-8, Elemane 523-47-7, β-Cadinene 555-10-2, β-Phellandrene 562-74-3, Terpinen-4-ol 1335-14-4 1674-08-4, trans-Pinocarveol 1820-09-3, trans-Ver-benol 2867-05-2, α-Thujene 3856-25-5, α-Copaene 4602-84-0, Farnesol 5208-59-3, β-Bourbonene 6753-98-6, Humulene 6895-56-3, β-Bergamotene 7663-66-3, Bergamotane 8007-35-0, Terpinyl acetate 8013-00-1, Terpinene 10178-38-8, Echinodol 14998-63-1D, Rhenium-186, etidronate complexes, biological studies 17627-44-0, α-Bisabolene 18794-84-8, β-Farnesene 19912-61-9, Furanodiene 20479-06-5, β-Ylangene 21698-66-8, Incensole oxide 21698-67-9, Incensole oxide acetate 22419-74-5, Incensole 25269-16-3, Isocembrene 25322-68-3D, conjugates with pyridoxylated Hb 28028-64-0, Germacrene 29063-28-3, Octanol 29350-73-0, Cadinene 31570-39-5, Cembrene-A 34701-53-6 35731-88-5, Isoincensole oxide 67921-02-2, Cembrenol 94325-73-2 94325-73-2D, compds. 122537-31-9, Oplopane 441771-56-8, Isoincensole 441771-57-9, Isoincensole acetate 441771-74-0, SKB 4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 141436-78-4, Protein kinase C

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitor, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 52660-18-1, Casein kinase 1 366806-33-9, Casein kinase 2
RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors (ICOS), pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 144114-21-6, **HIV**-1 Protease
RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors, pharmaceutical formulation further containing; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 70-18-8, Glutathione, biological studies 9030-21-1, Purine nucleoside phosphorylase 9040-48-6, Gelatinase 79747-53-8, Protein tyrosine phosphatase 79955-99-0, Stromelysin 80449-02-1, Tyrosine kinase 106096-93-9, Basic fibroblast growth factor 120178-12-3, Telomerase 131384-38-8, Ras farnesyltransferase 140879-24-9, Proteasome 141256-52-2, Matrilysin 141907-41-7, Matrix metalloproteinase 375798-61-1, Phosphatase, phosphoprotein
RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 10102-43-9, Nitric oxide, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study) (modulators, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 9002-61-3, Chorionic gonadotrophin
RL: BSU (Biological study, unclassified); BIOL (Biological study) (monoclonal antibody to human, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 9068-38-6, Reverse transcriptase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (nonnucleoside inhibitors of, pharmaceutical formulation further containing; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 1406-18-4, Vitamin E
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (oil, as pharmaceutical carrier; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 54-05-7, Chloroquine 54-42-2, Idoxuridine 60-54-8, Tetracycline 69-74-9, Cytarabine Hydrochloride 70-00-8, Trifluridine 80-08-0, Dapsone 90-34-6, Primaquine 100-33-4, Pentamidine 130-95-0, Quinine 443-48-1, Metronidazole 494-79-1, Melarsoprol 665-66-7, Amantadine Hydrochloride 1501-84-4, Rimantadine Hydrochloride 1910-68-5, Methisazone 3056-17-5, d4T 3736-81-0, Diloxanide furoate 5536-17-4, Vidarabine 7481-89-2, DdC 8064-90-2 9004-70-0, HE-2000 10500-82-0, Famotine Hydrochloride 10540-97-3, Memotine Hydrochloride 11006-77-2, Statolon 15176-29-1, Edoxudine 15185-43-0, DOTC 19387-91-8, Tinidazole 19885-51-9, Aranotin 22994-85-0, Benznidazole 23256-30-6, Nifurtimox 25526-93-6, Alovudine 27591-69-1, Tilorone Hydrochloride 27762-78-3, Kethoxal 29984-33-6, Vidarabine Phosphate 30516-87-1, AZT 35607-20-6, Avridine 36791-04-5, Ribavirin 36983-81-0, Fosfonet Sodium 37338-39-9 39809-25-1, Penciclovir 51867-87-9 53230-10-7, Mefloquine 56219-57-9, Arildone 59277-89-3, Acyclovir 63198-97-0, Viroxime 63585-09-1, Foscarnet Sodium 63968-64-9D, Artemisinin, derivs. 68693-30-1, Somantadine Hydrochloride 69123-90-6, Fiacitabine 69123-98-4, Fialuridine 69655-05-6, DdI 69657-51-8, Acyclovir Sodium 69756-53-2, Halofantrine 72301-78-1, Zinviroxime 72301-79-2, Enviroxime 73514-87-1, Fosarilate 77181-69-2, Sorivudine 80883-55-2, Enviradene 82410-32-0, Ganciclovir 84408-37-7, Desciclovir 85087-20-3, Doxycycline 87495-31-6, Disoxaril 95233-18-4, Atovaquone 100817-46-7, Stibogluconic acid 104227-87-4, Famciclovir 106362-32-7, Peptide T 106941-25-7, PMEA 107910-75-8, Ganciclovir Sodium 110042-95-0, Acemannan 110143-10-7, Lodenosine 113852-37-2, Cidofovir 124436-59-5, Pirodavir 124832-27-5, Valacyclovir Hydrochloride 127759-89-1, Lobucavir 127779-20-8, Saquinavir 129618-40-2, Nevirapine 132210-43-6, Cipamfylline 134678-17-4, 3TC 136470-78-5, Abacavir 136817-59-9, Delavirdine 137487-62-8, Alvircept Sudotox 138540-32-6,

Atevirdine Mesylate 141204-94-6, Co-artemether 142340-99-6
142632-32-4, Calanolide A 143491-57-0, Coviracil 145514-04-1, DAPD
147127-20-6, Tenofovir 147221-93-0, Delavirdine Mesylate 147318-81-8,
KNI-272 147362-57-0, Loviride 149845-06-7, Saquinavir Mesylate
149950-60-7, Emivirine 150378-17-9, Indinavir 153127-49-2, ALX40-4C
154598-52-4, DMP 266 155148-31-5, AMD 3100 155213-67-5, Ritonavir
156879-70-8 159519-65-0, Pentafuside 159989-64-7, Nelfinavir
163451-80-7 170020-61-8, FP-21399 174484-41-4, Tipranavir
177932-89-7, DMP-450 178979-85-6, AG 1549 185220-03-5, PNU142721
192725-17-0, ABT-378 214287-88-4, DPC961 216863-66-0, L-756423
251562-00-2, T-1249 383198-56-9, BW 141 383198-57-0, BMS-232630
383198-58-1, PRO 542
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(pharmaceutical formulation further containing; incensole and
furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 50-07-7, Mutamycin 50-18-0, Cyclophosphamide 50-28-2, Estradiol,
biological studies 50-35-1, Thalidomide 50-76-0, Dactinomycin
50-91-9, Floxuridine 51-21-8, Fluorouracil 51-75-2, Mechlorethamine
52-24-4, Thiotepa 53-19-0, Mitotane 53-43-0, DHEA 53-79-2, Puromycin
54-71-7, Pilocarpine hydrochloride 54-91-1, Pipobroman 55-21-0D,
Benzamide, N-substituted compds. 55-86-7, Mechlorethamine Hydrochloride
55-86-7D, Nitrogen mustard, derivs. 55-98-1, Busulfan 56-53-1,
Diethylstilbestrol 57-22-7, Vincristine 57-63-6, Ethinyl oestradiol
57-83-0, Progesterone, biological studies 58-05-9, Leucovorin 58-58-2,
Puromycin Hydrochloride 59-05-2, Methotrexate 66-75-1, Uracil Mustard
83-89-6, Acriquine 101-60-0, Porphyrin 106-60-5, Aminolevulinic acid
114-70-5, Sodium phenylacetate 122-79-2, Phenylacetate 125-45-1,
Azetepa 125-84-8, Aminoglutethimide 127-07-1, Hydroxyurea 143-67-9,
Vinblastine Sulfate 145-63-1, Suramin 147-94-4, Cytarabine 148-82-3,
Melphalan 154-42-7, Thioguanine 154-93-8, Carmustine 302-49-8,
Uredepa 302-79-4, Tretinoin 305-03-3, Chlorambucil 320-67-2,
Azacitidine 359-83-1, Pentazocine 364-62-5, Metoclopramide 366-70-1,
Procarbazine Hydrochloride 378-44-9, Betamethasone 423-55-2,
Perflubron 459-86-9, Mitoguazone 465-65-6, Naloxone 472-15-1,
Betulinic acid 481-29-8, Epiandrosterone 518-28-5, Podophyllotoxin
520-85-4, Medroxyprogesterone 521-12-0, Dromostanolone Propionate
536-59-4, Perillyl alcohol 548-04-9, Hypericin 566-48-3, Formestane
569-57-3, Chlorotrianisene 578-95-0D, Acridone, imidazo derivs.
578-95-0D, Acridone, propylbis derivs. 595-33-5, Megestrol Acetate
645-05-6, Altretamine 646-08-2, β-Alethine 671-16-9, Procarbazine
801-52-5, Porfiromycin 865-21-4, Vinblastine 911-45-5,
**Clomifene** 968-93-4, Testolactone 1271-19-8, Titanocene
dichloride 1402-81-9, Ambomycin 1403-99-2, Mitogillin 1404-00-8,
Mitomycin 1404-15-5, Nogalamycin 1404-20-2, Peliomycin 1404-64-4,
Sparsomycin 1661-29-6, Meturedepa 1972-08-3, Dronabinol 1980-45-6,
Benzodepa 2068-78-2, Vincristine Sulfate 2353-33-5, Decitabine
2508-89-6 2608-24-4, Piposulfan 2809-21-4D, Etidronic acid,
rhenium-186 complexes 2919-66-6, Melengestrol acetate 2998-57-4,
Estramustine 2998-57-4D, Estramustine, analogs 3073-59-4,
Hexamethylene bisacetamide 3094-09-5, Doxifluridine 3562-63-8,
Megestrol 3778-73-2, Ifosfamide 3930-19-6, Streptonigrin 4105-38-8
4291-63-8, Cladribine 4342-03-4, Dacarbazine 4342-07-8 4803-27-4,
Anthramycin 5072-26-4, Buthionine sulfoximine 5373-42-2, Thaliblastine
5508-58-7, Andrographolide 5579-27-1, Simtrazene 5581-52-2,
Thiamiprine 5696-17-3, Epipropidine 6157-87-5, Trestolone Acetate
7281-31-4, Vinglycinate Sulfate 7440-06-4D, Platinum, lipophilic compds.
or complexes 7440-06-4D, Platinum, triamine complexes 7644-67-9,
Azotomycin 7689-03-4D, Camptothecin, derivs. 7724-76-7, Riboprine
7761-45-7, Metoprine 8052-16-2, Cactinomycin 9002-71-5,
Thyroid-stimulating hormone 9014-02-2, Zinostatin 9014-42-0,
Thrombopoietin 9014-42-0D, Thrombopoietin, mimetics 9015-68-3,
Asparaginase 9027-98-9 9041-93-4, Bleomycin Sulfate 9050-67-3,
Sizofiran 10043-49-9, Gold-198, biological studies 10087-89-5,
Enpromate 10318-26-0, Mitolactol 10403-51-7, Mitindomide 10540-29-1,
Tamoxifen 11002-22-5, Apurinic acid 11029-06-4, Elemene 11043-98-4,
Mitocromin 11043-99-5, Mitomalcin 11056-06-7, Bleomycin 11056-12-5,
Cirolemycin 11056-14-7, Mitocarcin 11056-15-8, Mitosper 12713-07-4D,
Verdin, compds. 13010-47-4, Lomustine 13311-84-7, Flutamide

13494-90-1, Gallium nitrate 13665-88-8, Mopidamol 13909-09-6, Semustine 14769-73-4, Levamisole 15475-56-6, Methotrexate Sodium 15639-50-6, Safingol 15663-27-1, Cisplatin 17021-26-0, Calusterone 17902-23-7, Tegafur 18378-89-7, Plicamycin 18416-85-8, Lombricine 18556-44-0, Vinrosidine Sulfate 18588-57-3, Etoprine 18883-66-4, Streptozocin 19916-73-5, O6-Benzylguanine 20098-14-0, Idramantone 20537-88-6, Amifostine 20638-84-0, Retinamide 20830-81-3, Daunorubicin 21059-48-3, Veramine 21679-14-1, Fludarabine 22668-01-5, Etanidazole 23214-92-8, Doxorubicin 23541-50-6, Daunorubicin Hydrochloride 23593-75-1, Clotrimazole 24280-93-1, Mycophenolic Acid 24584-09-6, Dexrazoxane 25316-40-9, Adriamycin 27302-90-5, Oxisuran 27314-97-2, Tirapazamine 27548-93-2D, Baccatin III, derivs. 27686-84-6, Masoprocol 29069-24-7, Prednimustine 29767-20-2, Teniposide 30303-65-2, Docosanol 30387-51-0, Asperlin 30868-30-5, Pyrazofurin 31430-18-9, Nocodazole 31441-78-8, Mercaptopurine 32954-58-8, Ipomeanol 33069-62-4, Paclitaxel 33069-62-4D, Paclitaxel, analogs and derivs. 33419-42-0, Etoposide 35301-24-7, Cedefingol 35846-53-8, Maytansine 35943-35-2, Triciribine 36508-71-1, Zorubicin Hydrochloride 37717-21-8, Flurocitabine 38270-90-5, Strontium Chloride Sr 89 38321-02-7, Dexverapamil 39325-01-4, Picibanil 40391-99-9, Pamidronic acid 41575-94-4, Carboplatin 41729-52-6, Dezaguanine 41992-22-7, Spirogermanium Hydrochloride 42228-92-2, Acivicin 42616-25-1, Methioninase 50264-69-2, Lonidamine 51264-14-3, Amsacrine 51321-79-0, Sparfosic acid 52128-35-5, Trimetrexate 52205-73-9, Estramustine Phosphate Sodium 52794-97-5, Carubicin Hydrochloride 53643-48-4, Vindesine 53714-56-0, Leuprolide 53910-25-1, Pentostatin 54081-68-4, Vinleurosine Sulfate 54824-17-8, Mitonafide 55435-65-9, Acodazole Hydrochloride 56390-09-1, Epirubicin Hydrochloride 56420-45-2, Epirubicin 56605-16-4, Spiromustine 56741-95-8, Bropirimine 57381-26-7, Irsogladine 57576-44-0, Aclarubicin 57773-63-4, Triptorelin 57773-65-6, Deslorelin 57852-57-0, Idamycin 57998-68-2, Diaziquone 58066-85-6, Miltefosine 58525-82-9, Azatyrosine 58957-92-9, Idarubicin 58970-76-6, Ubenimex 59653-73-5, Teroxirone 59917-39-4, Vindesine Sulfate 59989-18-3, 5-Ethynyluracil 60084-10-8, Tiazofurin 60203-57-8, Prostaglandin J2 60940-34-3, Ebselen 61825-94-3, Oxaliplatin 61966-08-3, Triciribine Phosphate 62304-98-7, Thymalfasin 62435-42-1, Perfosfamide 62488-57-7 62816-98-2, Ormaplatin 62928-11-4, Iproplatin 63590-19-2, Balanol 63612-50-0, Nilutamide 63950-06-1, Esorubicin Hydrochloride
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 65057-90-1, Talisomycin 65093-40-5, Cytarabine ocfosfate 65222-35-7, Pazelliptine 65271-80-9, Mitoxantrone 65646-68-6, Fenretinide 65807-02-5, Goserelin 65886-71-7, Fazarabine 66569-27-5, Sparfosate Sodium 66849-34-1, Dexifosfamide 67699-41-6, Vinzolidine Sulfate 68278-23-9, Eflornithine Hydrochloride 68475-42-3, Anagrelide 69839-83-4, Didox 70052-12-9, Eflornithine 70384-29-1, Peplomycin Sulfate 70476-82-3, Mitoxantrone Hydrochloride 70641-51-9, Edelfosine 70711-40-9, Ametantrone Acetate 71294-60-5, Rohitukine 71439-68-4, Bisantrene Hydrochloride 71486-22-1, Vinorelbine 71522-58-2, Forfenimex 71628-96-1, Menogaril 72238-02-9D, Retelliptine, demethyl derivs. 72496-41-4, Pirarubicin 72629-69-7, Sarcophytol A 72732-56-0, Piritrexim 72741-87-8, Swainsonine 73105-03-0, Pentamustine 74149-70-5, Parabactin 74381-53-6, Leuprolide Acetate 74790-08-2, Spiroplatin 75219-46-4, Atrimustine 75330-75-5, Lovastatin 75607-67-9, Fludarabine Phosphate 75775-33-6D, Purpurin, compds. 75957-60-7, Splenopentin 76932-56-4, Nafarelin 77016-85-4, Plomestane 77327-05-0, Didemnin B 77599-17-8, Panomifene 77858-21-0, Velaresol 78113-36-7, Romurtide 78186-34-2, Bisantrene 79778-41-9, Neridronic acid 79831-76-8, Castanospermine 80451-05-4, Cecropin B 80576-83-6, Edatrexate 80663-95-2 80841-47-0, Asulacrine 81424-67-1, Caracemide 81965-43-7, SarCNU 82230-03-3, Carbetimer 82413-20-5, Droloxifene 82707-54-8, Neutral endopeptidase 82855-09-2D, Combretastatin, analogs 82952-64-5, Trimetrexate Glucuronate 83086-73-1, Tubulozole Hydrochloride 83150-76-9, Octreotide 83200-11-7, Vinepidine Sulfate 83519-04-4, Ilmofosine 83997-75-5, Iododoxorubicin 84030-84-2, Telluropyrylium 84088-42-6, Roquinimex 84371-65-3, Mifepristone

84412-94-2, Ruboxyl 85465-82-3, Thymotrinan 85622-93-1, Temozolomide
85754-59-2, Ambamustine 85969-07-9, Budotitane 85977-49-7,
Tauromustine 86976-56-9, Betaclamycins 87005-03-6, Panaxytriol
87434-82-0, Dezaguanine Mesylate 87806-31-3, Porfimer Sodium
87810-56-8, Fostriecin 87860-39-7, Fostriecin Sodium 88303-60-0,
Losoxantrone 88303-61-1, Losoxantrone Hydrochloride 89565-68-4,
Tropisetron 89778-26-7, Toremifene 89778-27-8, Toremifene Citrate
90357-06-5, Bicalutamide 90996-54-6, Rhizoxin 92047-76-2,
Tetrachlorodecaoxide 92118-27-9, Fotemustine 92788-10-8, Rogletimide
92803-82-2, Aphidicolin glycinate 94079-80-8, Cicaprost 95058-81-4,
Gemcitabine 95734-82-0, Nedaplatin 95933-72-5, Amidox 96201-88-6,
Brequinar Sodium 96301-34-7, Atamestane 96346-61-1, Onapristone
96389-68-3, Crisnatol 96389-69-4, Crisnatol Mesylate 96392-96-0,
Dexormaplatin 96892-57-8, Hepsulfam 97068-30-9, Elsamitrucin
97534-21-9, Merbarone 97682-44-5, Irinotecan 97752-20-0, Droloxifene
Citrate 97919-22-7 98319-26-7, Finasteride 98383-18-7, Ecomustine
98631-95-9, Sobuzoxane 99009-20-8, Pyrazoloacridine 99011-02-6,
Imiquimod 99283-10-0, Molgramostim 99614-02-5, Ondansetron
100286-90-6, Irinotecan Hydrochloride 100324-81-0, Lisofylline
102396-24-7, Jasplakinolide 102676-31-3, Fadrozole Hydrochloride
102676-47-1, Fadrozole 102822-56-0, Mannostatin A 103222-11-3,
Vapreotide 103612-80-2 104493-13-2, Adecypenol 105118-12-5,
Piroxantrone Hydrochloride 105149-04-0, Osaterone 105615-58-5,
Oxaunomycin 105844-41-5, Plasminogen activator inhibitor 106096-93-9D,
Basic Fibroblast growth factor, saporin conjugates 106400-81-1,
Lometrexol 107000-34-0, Zanoterone 107256-99-5, Tamoxifen methiodide
107868-30-4, Exemestane 108736-35-2, Lanreotide 108852-90-0,
Nemorubicin 109837-67-4, Cycloplatam 110267-81-7, Amrubicin
110311-27-8, Sulofenur 110314-48-2, Adozelesin 110690-43-2, Emitefur
110942-02-4, Aldesleukin 110942-08-0, Luprolide 111490-36-9,
Zeniplatin 111523-41-2, Enloplatin 112515-43-2, Topsentin
112522-64-2, Acetyldinaline 112809-51-5, Letrozole 112859-71-9,
Fluasterone 112887-68-0, Raltitrexed 112965-21-6, Calcipotriol
114084-78-5, Ibandronic acid 114285-68-6, Lentinan sulfate
114517-02-1, Fosquidone 114977-28-5, Taxotere 115150-59-9, Antagonist
G 115308-98-0, Tallimustine 115566-02-4, Bistratene A 115575-11-6,
Liarozole 115956-12-2, Dolasetron 116057-75-1, Idoxifene
117048-59-6, Combretastatin A4 117091-64-2, Etoposide Phosphate
118292-40-3, Tazarotene 119169-78-7, Epristeride 119413-54-6,
Topotecan Hydrochloride 119813-10-4, Carzelesin 120287-85-6,
Cetrorelix 120408-07-3, Lometrexol Sodium 120500-15-4, Leinamycin
120511-73-1, Anastrozole 120685-11-2, Benzoylstaurosporine
121181-53-1, Filgrastim 121263-19-2, Calphostin C 121288-39-9,
Loxoribine 121547-04-4, Mirimostim 122111-03-9, Gemcitabine
Hydrochloride 122341-38-2, Temoporfin 122431-96-3 122898-63-9,
Phenazinomycin 123040-69-7, Azasetron 123258-84-4, Itasetron
123760-07-6, Zinostatin stimalamer 123774-72-1, Sargramostim
123830-79-5, Teloxantrone Hydrochloride 123948-87-8, Topotecan
124012-42-6, Galocitabine 124689-65-2D, Cryptophycin A, derivs.
124784-31-2, Erbulozole 124904-93-4, Ganirelix 125317-39-7,
Vinorelbine Tartrate 125392-76-9, Acylfulvene 125533-88-2, Mofarotene
126297-39-0, Lissoclinamide 7 126443-96-7, Napavin 127984-74-1,
Lanreotide Acetate 128505-88-4, Naphterpin 128768-09-2, Placetin A
128768-11-6, Placetin B 129497-78-5, Verteporfin 129564-92-7, Azatoxin
129655-21-6, Bizelesin 129731-10-8, Vorozole 130167-69-0, Pegaspargase
130288-24-3, Duocarmycin SA 130364-39-5, Rubiginone B1 130370-60-4,
Batimastat 131190-63-1, Saintopin 132036-88-5, Ramosetron
132073-72-4, Tetrazomine 133432-71-0, Peldesine 134088-74-7,
Nartograstim 134381-30-9, Conagenin 134523-84-5 134633-29-7,
Tecogalan Sodium 134861-62-4, Dioxamycin 135257-45-3, Crambescidin 816
135381-77-0, Flezelastine 135383-02-7, Stipiamide 135558-11-1,
Lobaplatin 135819-69-1 135968-09-1, Lenograstim 137018-54-3,
Okicenone 137099-09-3, Turosteride 137219-37-5, Dehydrodidemnin B
137647-92-8, Axinastatin 1 137964-32-0 139755-79-6, Safingol
Hydrochloride 140207-93-8, Pentosan polysulfate sodium 140703-49-7,
Meterelin 142880-36-2, Ilomastat 144885-51-8, Sodium borocaptate
144916-42-7, Sonermin 145124-30-7, Bisnafide dimesylate 145858-50-0,
Liarozole Hydrochloride 146426-40-6, Flavopiridol 148317-76-4, Oracin
148584-53-6 148717-58-2, Palauamine 148717-90-2, Squalamine

149204-42-2, Kahalalide F
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 149260-80-0, Mycaperoxide B 149355-77-1, Lamellarin-N triacetate 149633-91-0, Leptolstatin 149715-96-8, Spongistatin 1 149882-10-0, Lurtotecan 150829-93-9, Nisamycin 151272-78-5, Antarelix 152923-56-3, Dacliximab 153723-34-3, Axinastatin 2 153723-35-4, Axinastatin 3 154039-60-8, Marimastat 154229-19-3, Abiraterone 154248-96-1, Iroplact 154277-21-1, Cypemycin 154361-50-9, Capecitabine 155233-30-0, Curacin A 156586-89-9, Edrecolomab 156790-85-1, Variolin B 156856-30-3, Cytostatin 157078-48-3, Isohomohalichondrin B 157857-21-1, Maspin 158792-24-6, Collismycin A 158792-25-7, Collismycin B 168482-36-8, Cryptophycin 8 172793-30-5 173046-02-1, Thiocoraline 174305-65-8, Breflate 181887-82-1, Nitrullin 188364-40-1, CARN 700 200139-38-4, Suradista 212894-59-2, Pentrozole 246252-04-0, Lutetium texaphyrin 246252-06-2, Gadolinium texaphyrin 284041-10-7 324740-00-3, Vitaxin 441070-87-7, 1,2,3-Triazolecarboxamide 441070-88-8 441070-92-4 441772-39-0, Isobengazole 441772-43-6, Nagrestip 441772-66-3, Vinxaltine 441772-81-2, Sulfmosine 441774-07-8, Spicamycin D 441774-77-2, Solverol
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 60529-76-2, Thymopoietin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(receptor agonists, pharmaceutical formulation further including; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 79217-60-0, Cyclosporin
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(treatment of immunodysregulation condition caused by treatment with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

IT 1397-89-3, Amphotericin B
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of immunodysregulation condition caused by treatment with; incensole and furanogermacrens and compds. as antitumor and antimicrobial agents)

L27 ANSWER 7 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:293427 CAPLUS
DOCUMENT NUMBER: 129:8597
TITLE: Embedding and encapsulation of controlled release particles
INVENTOR(S): Van Lengerich, Bernhard H.
PATENT ASSIGNEE(S): Van Lengerich, Bernhard H., USA
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9818610 | A1 | 19980507 | WO 1997-US18984 | 19971027 |
| W: AU, CA, JP, NO, PL, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| CA 2269806 | AA | 19980507 | CA 1997-2269806 | 19971027 |
| CA 2269806 | C | 20060124 | | |
| AU 9749915 | A1 | 19980522 | AU 1997-49915 | 19971027 |
| AU 744156 | B2 | 20020214 | | |
| EP 935523 | A1 | 19990818 | EP 1997-912825 | 19971027 |
| EP 935523 | B1 | 20040929 | | |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

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| JP 2002511777 | T2 | 20020416 | JP 1998-520558 | 19971027 |
| EP 1342548 | A1 | 20030910 | EP 2003-10031 | 19971027 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| AT 277739 | E | 20041015 | AT 1997-912825 | 19971027 |
| NO 9902036 | A | 19990428 | NO 1999-2036 | 19990428 |
| PRIORITY APPLN. INFO.: | | | US 1996-29038P | P 19961028 |
| | | | US 1997-52717P | P 19970716 |
| | | | EP 1997-912825 | A3 19971027 |
| | | | WO 1997-US18984 | W 19971027 |

AB Controlled release, discrete, solid particles which contain an encapsulated and/or embedded component such as a heat sensitive or readily oxidizable pharmaceutically, biol., or nutritionally active component are continuously produced without substantial destruction of the matrix material or encapsulant. A release-rate controlling component is incorporated into the matrix to control the rate of release of the encapsulant from the particles. The addnl. component may be a hydrophobic component or a high water binding capacity component for extending the release time. The plasticizable matrix material, such as starch, is admixed with at least one plasticizer, such as water, and at least one release-rate controlling component under low shear mixing conditions to plasticize the plasticizable material without substantially destroying the at least one plasticizable material and to obtain a substantially homogeneous plasticized mass. The plasticizer content is substantially reduced and the temperature of the plasticized mass is substantially reduced prior to admixing the plasticized mass with the encapsulant to avoid substantial destruction of the encapsulant and to obtain a formable, extrudable mixture The mixture is extruded though a die without substantial or essentially no expansion and cut into discrete, relatively dense particles. Release properties may also be controlled by precoating the encapsulant and/or coating the extruded particles with a film-forming component. An example of encapsulation of acetylcysteine is given using starch, polyethylene, glycerol monostearate, and vegetable oil.

IT Drug delivery systems
(controlled-release; embedding and encapsulation of controlled release particles)

IT Antitumor agents
Antiviral agents
Encapsulation
(embedding and encapsulation of controlled release particles)

IT Estrogens
Polyoxyalkylenes, biological studies
Tuberculin
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(embedding and encapsulation of controlled release particles)

IT Antibiotics
Antioxidants
Detergents
Emulsifying agents
Extrusion, nonbiological
Fats and Glyceridic oils, biological studies
Fatty acids, biological studies
Flavor
Fungicides
Glass transition
Heat treatment
Herbicides
Hydrocolloids
Insecticides
Lipids, biological studies
Paraffin waxes, biological studies
Peptides, biological studies
Perfumes
Pesticides
Plasticizers
Polyolefins

Polyurethanes, biological studies
Proteins, general, biological studies
Rodenticides
Steroids, biological studies
Surfactants
Waxes
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(embedding and encapsulation of controlled release particles)

IT Antibodies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal; embedding and encapsulation of controlled release particles)

IT Drug delivery systems
(particles; embedding and encapsulation of controlled release particles)

IT 50-02-2, Dexamethasone 50-04-4, Cortisone acetate 50-06-6, Phenobarbital, biological studies 50-12-4, Mephenytoin 50-14-6, Ergocalciferol 50-18-0, Cyclophosphamide 50-23-7, Hydrocortisone 50-24-8, Prednisolone 50-27-1, Estriol 50-28-2, Estradiol, biological studies 50-33-9, Phenylbutazone, biological studies 50-36-2, Cocaine 50-41-9, **Clomiphene** citrate 50-44-2, Mercaptopurine 50-47-5, Desipramine 50-48-6, Amitriptyline 50-49-7, Imipramine 50-52-2, Thioridazine 50-53-3, Chlorpromazine, biological studies 50-54-4, Quinidine sulfate 50-55-5, Reserpine 50-58-8, Phendimetrazine tartrate 50-63-5, Chloroquine phosphate 50-78-2, Acetylsalicylic acid 50-81-7, Ascorbic acid, biological studies 50-96-4, Isoetharine hydrochloride 51-05-8, Procaine hydrochloride 51-15-0, Pralidoxime chloride 51-21-8, Fluorouracil 51-30-9, Isoproterenol hydrochloride 51-34-3, Scopolamine 51-43-4, Epinephrine 51-48-9, Levothyroxine, biological studies 51-52-5, Propylthiouracil 51-55-8, Atropine, biological studies 51-57-0, Methamphetamine hydrochloride 51-64-9, Dextroamphetamine 51-83-2, Carbachol 51-84-3, Acetylcholine, biological studies 51-98-9, Norethindrone acetate 52-01-7, Spironolactone 52-24-4, Thiotepa 52-49-3, Trihexyphenidyl hydrochloride 52-53-9, Verapamil 52-67-5, Penicillamine 52-68-6, Trichlorfon 52-86-8, Haloperidol 52-89-1, Cysteine hydrochloride 53-03-2, Prednisone 53-16-7, Estrone, biological studies 53-19-0, Mitotane 53-39-4, Oxandrolone 53-60-1, Promazine hydrochloride 53-86-1, Indomethacin 54-21-7, Sodium salicylate 54-31-9, Furosemide 54-36-4, Metyrapone 54-64-8, Thimerosal 54-85-3, Isoniazid 55-03-8, Levothyroxine sodium 55-06-1, Liothyronine sodium 55-63-0, Nitroglycerin 55-98-1, Busulfan 56-29-1, Hexobarbital 56-47-3, Desoxycorticosterone acetate 56-53-1, Diethylstilbestrol 56-54-2, Quinidine 56-75-7, Chloramphenicol 56-84-8, L-Aspartic acid, biological studies 56-87-1, L-Lysine, biological studies 57-13-6, Urea, biological studies 57-22-7, Vincristine 57-33-0, Pentobarbital sodium 57-41-0, Phenytoin 57-42-1, Meperidine 57-43-2, Amobarbital 57-47-6, Physostigmine 57-53-4, Meprobamate 57-63-6, Ethinyl estradiol 57-66-9, Probenecid 57-68-1, Sulfamethazine 57-83-0, Progesterone, biological studies 57-92-1, Streptomycin, biological studies 57-96-5, Sulfinpyrazone 58-00-4, Apomorphine 58-08-2, Caffeine, biological studies 58-14-0, Pyrimethamine 58-18-4, Methyltestosterone 58-22-0 58-25-3, Chlordiazepoxide 58-27-5, Menadione 58-32-2, Dipyridamole 58-33-3, Promethazine hydrochloride 58-38-8, Prochlorperazine 58-39-9, Perphenazine 58-40-2, Promazine 58-54-8, Ethacrynic acid 58-55-9, Theophylline, biological studies 58-56-0, Pyridoxine hydrochloride 58-85-5, Biotin 58-89-9, Lindane 58-93-5, Hydrochlorothiazide 58-94-6, Chlorothiazide 59-05-2, Methotrexate 59-30-3, Folic acid, biological studies 59-33-6, Pyrilamine maleate 59-43-8, Thiamin, biological studies 59-52-9, Dimercaprol 59-63-2, Isocarboxazid 59-66-5, Acetazolamide 59-67-6, Niacin, biological studies 59-92-7, Levodopa, biological studies 60-13-9, Amphetamine sulfate 60-18-4, Tyrosine, biological studies 60-54-8, Tetracycline 60-56-0, Methimazole 60-80-0, Antipyrine 60-87-7, Promethazine 60-99-1, Levomepromazine 61-00-7, Acepromazine 61-25-6, Papaverine hydrochloride 61-68-7, Mefenamic acid 61-76-7, Phenylephrine hydrochloride 61-90-5, Leucine, biological studies 62-31-7, Dopamine hydrochloride 62-44-2, Phenacetin 62-67-9, Nalorphine 62-90-8, Nandrolone phenpropionate 63-68-3, Methionine, biological studies

63-91-2, Phenylalanine, biological studies 63-92-3, Phenoxybenzamine hydrochloride 63-98-9, Phenacemide 64-31-3, Morphine sulfate 64-72-2, Chlortetracycline hydrochloride 64-77-7, Tolbutamide 64-86-8, Colchicine 65-45-2, Salicylamide 66-76-2, Dicoumarol 67-03-8, Thiamine hydrochloride 67-20-9, Nitrofurantoin 67-45-8, Furazolidone 67-73-2, Fluocinolone acetonide 67-96-9, Dihydrotachysterol 67-97-0, Cholecalciferol 68-19-9, Cyanocobalamin 68-22-4, Norethindrone 68-35-9, Sulfadiazine 68-41-7, Cycloserine 68-89-3, Metamizole 69-23-8, Fluphenazine 69-44-3, Amodiaquine hydrochloride 69-53-4, Ampicillin 69-72-7, Salicylic acid, biological studies 71-00-1, Histidine, biological studies 71-58-9, Medroxyprogesterone acetate 71-63-6, Digitoxin 71-68-1, Hydromorphone hydrochloride 71-81-8 72-14-0, Sulfathiazole 72-17-3, Sodium lactate 72-18-4, Valine, biological studies 72-19-5, L-Threonine, biological studies 72-33-3, Mestranol 72-63-9, Methandrostenolone 73-22-3, L-Tryptophan, biological studies 73-48-3, Bendroflumethiazide 76-38-0, Methoxyflurane 76-42-6, Oxycodone 76-43-7, Fluoxymesterone 76-57-3, Codeine 77-09-8 77-19-0, Dicyclomine 77-21-4, Glutethimide 77-26-9, Butalbital 77-27-0, Thiamylal 77-36-1, Chlorthalidone 77-41-8, Methsuximide 78-44-4, Carisoprodol 79-57-2, Oxytetracycline 80-08-0, Dapsone 80-13-7, Halazone 80-53-5, Terpin 81-07-2, Saccharin 81-13-0, Dexpanthenol 81-23-2, Dehydrocholic acid 81-81-2, Warfarin 83-43-2, Methylprednisolone 83-73-8, Iodoquinol 83-88-5, Riboflavin, biological studies 84-02-6, Prochlorperazine maleate 84-17-3, Dienestrol 84-22-0, Tetrahydrozoline 84-80-0, Phytonadione 85-79-0, Dibucaine 86-35-1, Ethotoin 87-00-3, Homatropine 87-08-1, Phenoxymethylpenicillin 87-33-2, ISDN 89-57-6, 5-Aminosalicylic acid 90-33-5, Hymecromone 90-34-6, Primaquine 91-33-8, Benzthiazide 91-81-6, Tripelennamine 92-13-7, Pilocarpine 93-14-1, Guaifenesin 94-09-7, Benzocaine 94-20-2, Chlorpropamide 95-25-0, Chlorzoxazone 97-53-0, Eugenol 97-77-8, Disulfiram 98-96-4, Pyrazinamide 99-66-1, Valproic acid 100-97-0, biological studies 101-26-8, Pyridostigmine bromide 101-31-5, Hyoscyamine 102-76-1, Triacetin 103-16-2, Monobenzone 103-86-6, Hydroxyamphetamine 103-90-2, Acetaminophen 104-28-9, Cinoxate 104-31-4, Benzonatate 107-43-7, Betaine 108-46-3, 1,3-Benzenediol, biological studies 110-85-0, Piperazine, biological studies 110-94-1, Pentanedioic acid 113-18-8, Ethchlorvynol 113-52-0, Imipramine hydrochloride 113-59-7, Chlorprothixene 113-92-8, Chlorpheniramine maleate 114-07-8, Erythromycin 114-80-7, Neostigmine bromide 115-38-8, Mephobarbital 115-77-5, biological studies 120-97-8, Dichlorphenamide 121-25-5, Amprolium
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(embedding and encapsulation of controlled release particles)

IT 121-54-0 121-75-5, Malathion 123-31-9, 1,4-Benzenediol, biological studies 124-90-3, Oxycodone hydrochloride 124-94-7, Triamcinolone 125-28-0, Dihydrocodeine 125-33-7, Primidone 125-71-3, Dextromethorphan 125-72-4, Levorphanol tartrate 126-07-8, Griseofulvin 127-07-1, Hydroxyurea 127-33-3, Demeclocycline 127-48-0, Trimethadione 127-69-5, Sulfisoxazole 127-79-7, Sulfamerazine 128-44-9, Saccharin sodium 128-46-1, Dihydrostreptomycin 128-49-4, Docusate calcium 128-62-1, Noscapine 129-20-4, Oxyphenbutazone 129-49-7, Methysergide maleate 129-51-1, Ergonovine maleate 130-26-7, Clioquinol 130-61-0, Thioridazine hydrochloride 131-13-5 131-57-7, Oxybenzone 132-17-2 132-92-3, Methicillin sodium 133-58-4, Nitromersol 133-67-5, Trichlormethiazide 134-03-2, Sodium ascorbate 134-80-5, Diethylpropion hydrochloride 135-07-9 135-09-1, Hydroflumethiazide 136-40-3, Phenazopyridine hydrochloride 136-47-0 136-77-6, Hexylresorcinol 137-58-6, Lidocaine 141-01-5, Ferrous fumarate 143-71-5, Hydrocodone bitartrate 143-81-7, Butabarbital sodium 144-14-9, Anileridine 144-48-9, Iodoacetamide 144-55-8, Sodium bicarbonate, biological studies 144-80-9, Sulfacetamide 144-82-1, Sulfamethizole 144-83-2, Sulfapyridine 146-22-5, Nitrazepam 146-54-3, Triflupromazine 147-24-0, Diphenhydramine hydrochloride 147-52-4, Nafcillin 147-85-3, Proline, biological studies 148-79-8 148-82-3, Melphalan 151-67-7, Halothane 152-62-5, Dydrogesterone 152-97-6, Fluocortolone 154-41-6, Phenylpropanolamine hydrochloride 154-42-7, Thioguanine 156-51-4, Phenelzine sulfate 297-76-7, Ethynodiol diacetate 298-46-4, Carbamazepine 298-50-0, Propantheline 298-57-7, Cinnarizine

298-59-9, Methylphenidate hydrochloride 298-81-7, Methoxsalen
299-27-4, Potassium gluconate 299-29-6, Ferrous gluconate 299-42-3,
Ephedrin 302-22-7, Chlormadinone acetate 302-79-4, Tretinoin
303-25-3, Cyclizine hydrochloride 304-20-1, Hydralazine hydrochloride
304-59-6, Potassium sodium tartrate, biological studies 305-03-3,
Chlorambucil 309-43-3, Secobarbital sodium 315-30-0, Allopurinol
317-34-0, Aminophylline 318-98-9 329-65-7, 1,2-Benzenediol,
4-[1-hydroxy-2-(methylamino)ethyl]- 343-55-5, Dicloxacillin sodium
345-78-8, Pseudoephedrine hydrochloride 346-18-9, Polythiazide
356-12-7, Fluocinonide 357-07-3, Oxymorphone hydrochloride 359-83-1,
Pentazocine 360-70-3, Nandrolone decanoate 364-62-5, Metoclopramide
364-98-7, Diazoxide 366-70-1, Procarbazine hydrochloride 378-44-9,
Betamethasone 379-79-3, Ergotamine tartrate 382-67-2, Desoximetasone
389-08-2, Nalidixic acid 390-64-7, Prenylamine 396-01-0, Triamterene
426-13-1, Fluorometholone 434-07-1, Oxymetholone 435-97-2,
Phenprocoumon 437-74-1, Xantinol nicotinate 439-14-5, Diazepam
440-17-5, Trifluoperazine hydrochloride 443-48-1, Metronidazole
446-86-6, Azathioprine 465-65-6, Naloxone 466-99-9, Hydromorphone
471-34-1, Calcium carbonate, biological studies 474-86-2, Equilin
479-18-5, Dyphylline 484-23-1, Dihydralazine 486-12-4, Triprolidine
511-12-6, Dihydroergotamine 514-36-3, Fludrocortisone acetate
514-65-8, Biperiden 518-47-8, Fluorescein sodium 519-37-9, Etofylline
520-85-4, Medroxyprogesterone 523-87-5, Dimenhydrinate 525-66-6,
Propranolol 527-07-1, Sodium gluconate 532-03-6, Methocarbamol
533-45-9, Clomethiazole 536-21-0, Norfenefrine 536-33-4, Ethionamide
541-15-1, Levocarnitine 546-88-3, Acetohydroxamic acid 546-93-0,
Magnesium carbonate 548-62-9, Gentian violet 548-73-2, Droperidol
549-18-8, Amitriptyline hydrochloride 550-83-4, Propoxycaine
hydrochloride 551-27-9, Propicillin 552-94-3, Salsalate 554-13-2,
Lithium carbonate 554-57-4, Methazolamide 554-92-7, Trimethobenzamide
hydrochloride 555-30-6, Methyldopa 557-34-6, Zinc acetate 562-10-7
564-25-0, Doxycycline 577-11-7, Docusate sodium 579-56-6, Isoxsuprine
hydrochloride 587-61-1, Propyliodone 590-63-6, Bethanechol chloride
595-33-5, Megestrol acetate 596-51-0, Glycopyrrolate 599-79-1,
Sulfasalazine 599-88-2, Sulfaperin 603-50-9, Bisacodyl 604-75-1,
Oxazepam 614-39-1, Procainamide hydrochloride 616-91-1, Acetylcysteine
620-61-1, Hyoscyamine sulfate 630-56-8, Hydroxyprogesterone caproate
637-07-0, Clofibrate 637-58-1, Pramoxine hydrochloride 638-23-3
642-78-4, Cloxacillin sodium 651-06-9, Sulfamethoxydiazine 652-67-5
672-87-7, Metyrosine 709-55-7, Etilefrine 721-50-6, Prilocaine
723-46-6, Sulfamethoxazole 738-70-5, Trimethoprim 745-65-3,
Alprostadil 747-36-4, Hydroxychloroquine sulfate 768-94-5, Amantadine
777-11-7, Haloprogin 797-63-7, Levonorgestrel 826-39-1, Mecamylamine
hydrochloride 846-49-1, Lorazepam 846-50-4, Temazepam 859-18-7,
Lincomycin hydrochloride 865-21-4, Vinblastine 894-71-3, Nortriptyline
hydrochloride 968-81-0, Acetohexamide 968-93-4, Testolacton
969-33-5, Cyproheptadine hydrochloride 985-16-0, Nafcillin sodium
1069-66-5, Sodium valproate 1070-11-7, Ethambutol hydrochloride
1077-28-7, Thioctic acid 1094-08-2, Ethopropazine hydrochloride
1095-90-5, Methadone hydrochloride 1098-97-1, Pyritinol 1104-22-9,
Meclizine hydrochloride 1134-47-0, Baclofen 1143-38-0, Anthralin
1151-11-7, Ipodate calcium 1156-19-0, Tolazamide 1173-88-2, Oxacillin
sodium 1197-21-3, Phentermine hydrochloride 1221-56-3, Ipodate sodium
1225-55-4, Protriptyline hydrochloride 1229-29-4, Doxepin hydrochloride
1247-42-3, Meprednisone 1263-89-4, Paromomycin sulfate 1309-48-4,
Magnesium oxide, biological studies 1319-82-0, Aminocaproic acid
1321-23-9, Chloroxylenol 1343-97-1, Selenium sulfate 1393-48-2,
Thiostrepton 1400-61-9, Nystatin 1403-17-4, Candicidin 1403-66-3,
Gentamicin 1404-00-8, Mitomycin 1404-04-2, Neomycin 1404-88-2,
Tyrothricin 1404-93-9, Vancomycin hydrochloride 1405-10-3, Neomycin
sulfate 1405-20-5, Polymyxin b sulfate 1405-87-4, Bacitracin
1405-97-6, Gramicidin 1406-05-9, Penicillin 1420-55-9,
Thiethylperazine 1476-53-5, Novobiocin sodium 1492-18-8, Leucovorin
calcium 1508-65-2, Oxybutynin chloride 1508-75-4, Tropicamide
1508-76-5, Procyclidine hydrochloride 1524-88-5, Flurandrenolide
1597-82-6, Paramethasone acetate 1617-90-9, Vincamine 1622-61-3,
Clonazepam 1622-62-4, Flunitrazepam 1639-60-7, Propoxyphene
hydrochloride 1649-18-9, Azaperone 1668-19-5, Doxepin 1707-14-8,
Phenmetrazine hydrochloride 1808-12-4, Bromodiphenhydramine

hydrochloride 1812-30-2, Bromazepam 1897-96-7, Lonetil 1972-08-3, Dronabinol 1977-10-2, Loxapine
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(embedding and encapsulation of controlled release particles)

IT 1982-37-2, Methdilazine 2013-58-3, Meclocycline 2022-85-7, Flucytosine 2030-63-9, Clofazimine 2062-78-4, Pimozide 2098-66-0, Cyproterone 2179-37-5, Bencyclane 2192-20-3, Hydroxyzine hydrochloride 2315-02-8, Oxymetazoline hydrochloride 2398-96-1, Tolnaftate 2438-32-6, Dexchlorpheniramine maleate 2447-57-6, Sulfadoxine 2589-47-1, Prajmalium bitartrate, biological studies 2609-46-3, Amiloride 2709-56-0, Flupentixol 2898-12-6, Medazepam 2955-38-6, Prazepam 2998-57-4, Estramustine 3313-26-6, Thiothixene 3385-03-3, Flunisolide 3485-14-1, Cyclacillin 3485-62-9, Clidinium bromide 3486-35-9, Zinc carbonate 3505-38-2, Carbinoxamine maleate 3546-41-6, Pyrvinium pamoate 3572-43-8, Bromhexine 3575-80-2, Melperone 3625-06-7, Mebeverine 3632-91-5, Magnesium gluconate 3778-73-2, Ifosfamide 3810-80-8, Diphenoxylate hydrochloride 3902-71-4, Trioxsalen 3930-20-9, Sotalol 3963-95-9, Methacycline hydrochloride 3978-86-7, Azatadine maleate 4205-90-7, Clonidine 4205-91-8, Clonidine hydrochloride 4330-99-8, Trimeprazine tartrate 4468-02-4, Zinc gluconate 4498-32-2, Dibenzepine 4499-40-5, Oxtriphylline, biological studies 4697-36-3, Carbenicillin 4759-48-2, Isotretinoin 5051-62-7, Guanabenz 5104-49-4, Flurbiprofen 5321-32-4, Hetacillin potassium 5355-48-6 5370-01-4, Mexiletine hydrochloride 5534-09-8, Beclomethasone dipropionate 5536-17-4, Vidarabine 5636-83-9, Dimetindene 5638-76-6, Betahistine 5874-97-5, Metaproterenol sulfate 5875-06-9, Proparacaine hydrochloride 5987-82-6, Benoxinate hydrochloride 6202-23-9, Cyclobenzaprine hydrochloride 6284-40-8, Meglumine 6385-02-0, Meclofenamate sodium 6452-73-9, Oxprenolol hydrochloride 6493-05-6, Pentoxifylline 6533-00-2, Norgestrel 6805-41-0, Aescin 6890-40-0, Histamine phosphate 7054-25-3, Quinidine gluconate 7195-27-9, Mefruside 7235-40-7, β-Carotene 7246-21-1, Tyropanoate sodium 7280-37-7, Estropipate 7297-25-8, Erythrityl tetranitrate 7414-83-7, Etidronate disodium 7439-95-4D, Magnesium, salts, biological studies 7439-96-5, Manganese, biological studies 7439-96-5D, Manganese, salts, biological studies 7440-39-3, Barium, biological studies 7440-69-9, Bismuth, biological studies 7440-70-2, Calcium, biological studies 7447-40-7, Potassium chloride (KCl), biological studies 7491-74-9, Piracetam 7553-56-2, Iodine, biological studies 7632-00-0, Sodium nitrite 7646-85-7, Zinc chloride, biological studies 7681-11-0, Potassium iodide (KI), biological studies 7681-49-4, Sodium fluoride, biological studies 7681-82-5, Sodium iodide, biological studies 7681-93-8, Natamycin 7693-13-2, Calcium citrate 7720-78-7, Ferrous sulfate 7778-49-6, Potassium citrate 7783-00-8, Selenious acid 7786-30-3, Magnesium chloride, biological studies 8017-57-0, Trisulfapyrimidine 8024-48-4, Casanthranol 8049-47-6, Pancreatin 8050-81-5, Simethicone 8065-29-0, Liotrix 8067-24-1, Ergoloid mesylates 9001-01-8, Kallidinogenase 9001-73-4, Papain 9002-07-7, Trypsin 9002-60-2, Corticotropin, biological studies 9002-61-3, Chorionic gonadotropin 9002-86-2, Pvc 9002-89-5, Polyvinyl alcohol 9003-20-7, Polyvinyl acetate 9003-39-8, Pvp 9003-97-8, Polycarbophil 9004-07-3, Chymotrypsin 9004-10-8, Insulin, biological studies 9004-32-4, Carboxymethylcellulose 9004-34-6D, Cellulose, esters and ethers, biological studies 9004-53-9, Dextrin 9004-70-0, Pyroxylin 9005-25-8, Starch, biological studies 9005-80-5, Inulin 9008-05-3, Histoplasmin 10025-73-7, Chromic chloride 10040-45-6, Sodium picosulfate 10238-21-8, Glibenclamide 10246-75-0, Hydroxyzine pamoate 10262-69-8, Maprotiline 10347-81-6, Maprotiline hydrochloride 10379-14-3, Tetrazepam 10418-03-8, Stanozolol 10540-29-1, Tamoxifen 11000-17-2, Vasopressin 12125-02-9, Ammonium chloride, biological studies 12619-70-4, Cyclodextrin 12622-73-0, Coccidioidin 12633-72-6, Amphotericin 12650-69-0, Mupirocin 13009-99-9, Mafenide acetate 13042-18-7, Fendiline 13292-46-1, Rifampin 13311-84-7, Flutamide 13392-18-2, Fenoterol 13422-51-0, Hydroxocobalamin 13463-67-7, Titanium dioxide, biological studies 13523-86-9, Pindolol 13614-98-7, Minocycline hydrochloride 13682-92-3, Dihydroxyaluminum aminoacetate 14009-24-6, Drotaverine 14028-44-5, Amoxapine 14779-78-3, Padimate 14976-57-9, Clemastine fumarate 15078-28-1,

Nitroprusside 15307-86-5, Diclofenac 15622-65-8, Molindone hydrochloride 15663-27-1, Cisplatin 15676-16-1, Sulpiride 15686-51-8, Clemastine 15686-71-2, Cephalexin 15687-27-1 15687-41-9, Oxyfedrine 16482-55-6, Dihydroxyaluminum sodium carbonate 16595-80-5, Levamisole hydrochloride 16662-47-8, Gallopamil 17140-78-2, Propoxyphene napsylate 17230-88-5, Danazol 17560-51-9, Metolazone 17617-23-1, Flurazepam 18378-89-7, Plicamycin 18559-94-9, Salbutamol 19216-56-9, Prazosin 19237-84-4, Prazosin hydrochloride 19356-17-3, Calcifediol 20830-75-5, Digoxin 21462-39-5, Clindamycin hydrochloride 21738-42-1, Oxamniquine 21829-25-4, Nifedipine 22059-60-5, Disopyramide phosphate 22071-15-4, Ketoprofen 22195-34-2, Guanadrelsulfate 22204-24-6, Pyrantel pamoate 22204-53-1, Naproxen 22232-71-9, Mazindol 22260-51-1, Bromocriptine mesylate 22316-47-8, Clobazam 22494-42-4 22916-47-8 23031-25-6, Terbutaline 23031-32-5, Terbutaline sulfate 23214-92-8, Doxorubicin 23288-49-5, Probucol 23593-75-1, Clotrimazole 23869-24-1, O-(β-Hydroxyethyl)-rutoside 24219-97-4, Mianserin 24390-14-5, Doxycycline hyclate 24729-96-2, Clindamycin phosphate 25046-79-1, Glisoxepide 25086-89-9, Vinyl acetate-N-vinylpyrrolidinone copolymer 25155-18-4, Methylbenzethonium chloride 25167-80-0, Chlorophenol 25301-02-4, Tyloxapol 25322-68-3 25332-39-2, Trazodone hydrochloride 25389-94-0, Kanamycin sulfate 25614-03-3, Bromocriptine 25655-41-8, Povidone iodine 25717-80-0, Molsidomine 25812-30-0, Gemfibrozil 25953-19-9, Cefazolin 26027-38-3, Nonoxynol 9 26171-23-3, Tolmetin 26652-09-5, Ritodrine 26675-46-7, Isoflurane 26787-78-0, Amoxicillin 26807-65-8, Indapamide 26839-75-8, Timolol 26944-48-9, Glibornuride 27203-92-5, Tramadol 27823-62-7, Chlortetracycline bisulfate 28088-64-4, Aminosalicylic acid 28395-03-1, Bumetanide 28657-80-9, Cinoxacin 28797-61-7, Pirenzepine 28860-95-9, Carbidopa 28911-01-5, Triazolam 28981-97-7, Alprazolam 29122-68-7, Atenolol 29679-58-1, Fenoprofen 30578-37-1, Amezinium metilsulfate 30685-43-9, Metildigoxin 31329-57-4, Naftidrofuryl 31431-39-7, Mebendazole 31637-97-5, Etofibrate 31828-71-4, Mexiletine 32672-69-8, Mesoridazine besylate 32780-64-6, Labetalol hydrochloride 32887-01-7, Amdinocillin 33005-95-7, Tiaprofenic acid 33286-22-5, Diltiazem hydrochloride 33402-03-8, Metaraminol bitartrate 33419-42-0 33996-33-7, Oxaceprol 34031-32-8, Auranofin
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(embedding and encapsulation of controlled release particles)

IT 34183-22-7, Propafenone hydrochloride 34552-83-5, Loperamide hydrochloride 34580-13-7, Ketotifen 34787-01-4, Ticarcillin 36322-90-4, Piroxicam 36688-78-5 36791-04-5 37270-89-6, Heparin calcium 37517-28-5, Amikacin 37517-30-9, Acebutolol 38194-50-2, Sulindac 38260-01-4, Trientine hydrochloride 38304-91-5, Minoxidil 38363-40-5, Penbutolol 38396-39-3, Bupivacaine 38821-53-3, Cephradine 39562-70-4, Nitrendipine 40828-46-4, Suprofen 41859-67-0, Bezafibrate 42200-33-9, Nadolol 42399-41-7, Diltiazem 42540-40-9, Cefamandole nafate 49562-28-9, Fenofibrate 49745-95-1, Dobutamine hydrochloride 50370-12-2, Cefadroxil 50679-08-8, Terfenadine 50925-79-6, Colestipol 50972-17-3, Bacampicillin 51022-69-6, Amcinonide 51481-61-9, Cimetidine 51781-06-7, Carteolol 52468-60-7, Flunarizine 53164-05-9, Acemetacin 53179-11-6, Loperamide 53230-10-7, Mefloquine 53608-75-6, Pancrelipase 53994-73-3, Cefaclor 54063-53-5, Propafenone 54143-55-4, Flecainide 54182-58-0, Sucralfate 54965-21-8, Albendazole 54965-24-1, Tamoxifen citrate 55268-74-1, Praziquantel 55837-25-7, Buflomedil 55837-27-9, Piretanide 56392-17-7, Metoprolol tartrate 57109-90-7, Dipotassium chlorazepate 57432-61-8, Methylergonovine maleate 57435-86-6, Premazepam 58551-69-2, Carboprost tromethamine 59277-89-3, Acyclovir 59865-13-3, Cyclosporine 60166-93-0, Iopamidol 60200-06-8, Clorsulon 60833-22-9, Pyridoxal 5'-phosphate glutamate 61177-45-5, Clavulanate potassium 61489-71-2, Menotropin 61563-18-6, Soquinolol 62571-86-2, Captopril 62893-19-0, Cefoperazone 63527-52-6, Cefotaxime 63659-18-7, Betaxolol 64024-15-3, Pentazocine hydrochloride 64544-07-6, Cefuroxime axetil 65277-42-1, Ketoconazole 65666-07-1, Silymarin 65899-73-2, Tioconazole 66108-95-0, Iohexol 66357-35-5, Ranitidine 66711-21-5, Apraclonidine 66734-13-2, Alclometasone dipropionate 68844-77-9, Astemizole 70458-96-7, Norfloxacin 72558-82-8, Ceftazidime 74978-16-8, Magaldrate 75330-75-5, Lovastatin 76095-16-4, Enalapril maleate 76420-72-9,

Enalaprilat 76470-66-1, Loracarbef 76547-98-3, Lisinopril 76824-35-6, Famotidine 76963-41-2, Nizatidine 78110-38-0, Aztreonam 78266-06-5, Mebrofenin 79350-37-1, Cefixime 81103-11-9, Clarithromycin 83200-10-6, Anipamil 83905-01-5, Azithromycin 85721-33-1, Ciprofloxacin 92665-29-7, Cefprozil 102188-40-9, Acromycin 150977-36-9, Bromelain
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(embedding and encapsulation of controlled release particles)
IT 9001-92-7, Protease
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors, **HIV**; embedding and encapsulation of controlled release particles)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 8 OF 23 MEDLINE on STN
ACCESSION NUMBER: 91300152 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2070114
TITLE: Infertility management in **HIV** positive couples: a dilemma.
AUTHOR: Smith J R; Forster G E; Kitchen V S; Hooi Y S; Munday P E; Paintin D B
CORPORATE SOURCE: St Mary's Hospital, London.
SOURCE: BMJ (Clinical research ed.), (1991 Jun 15) Vol. 302, No. 6790, pp. 1447-50.
Journal code: 8900488. ISSN: 0959-8138.
Report No.: KIE-33645.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Bioethics; Priority Journals; AIDS
ENTRY MONTH: 199108
ENTRY DATE: Entered STN: 19910908
Last Updated on STN: 20030318
Entered Medline: 19910822

L27 ANSWER 9 OF 23 MEDLINE on STN
ACCESSION NUMBER: 91020580 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2219439
TITLE: Infertility: an approach to management in a district hospital in Ghana.
AUTHOR: Fiander A
CORPORATE SOURCE: Bawku Hospital, Upper East Region, Ghana.
SOURCE: Tropical doctor, (1990 Jul) Vol. 20, No. 3, pp. 98-100.
Journal code: 1301706. ISSN: 0049-4755.
Report No.: CPFH-27180cr990; POP-00195546.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Population
ENTRY MONTH: 199011
ENTRY DATE: Entered STN: 19910117
Last Updated on STN: 20021101
Entered Medline: 19901116
AB Up to 1/3 of women of child bearing age are infertile in certain African areas. Over 1000 patients registered at Bawku Hospital, Upper East Region, Ghana during an 18-month period, where a scheme for the investigation and treatment of infertile patients was established. The 5 main causes of infertility are: 1) tubal damage; 2) male factor; 3) anovulation; 4) uterine factor; and 5) unexplained. Special clinics are set up for infertility; outpatient staff are recruited. A preprinted questionnaire should be used for a uniform approach. The one used in Bawku is shown in the appendix. Health talks should be given. They should use the local language be at the right level, and use visual **aids**. In large clinics, numbers should be used to insure a 1st come, 1st served basis. A treatment protocol is important. When the

patient 1st walks in, the infertility form is completed; appropriate investigations are done--hemoglobin, VDRL, seminal analysis, and cervical or high vagina swabs, and others--and the results are reviewed. The patient is encouraged to keep a menstrual calendar for 3 months. At the 2nd visit, the menstrual calendar is reviewed. A pelvic examination and a tubal patency test (TPT) are done. At the 3rd visit, abdominal and pelvic examinations are done and a TPT. Then patients can be diagnosed and counselled accordingly. At the last visit, further explanation is given, further TPTs are done if necessary, and anovulation is treated with **clomiphene**. The visits are spread out over 6 months. In unexplained fertility cases, the couple is told there is nothing wrong, they should keep trying. The idea that the man may be causing the infertility is foreign to many communities. This needs changing. 20% of infertility is due to male factor in Bawku. Male infertility is hard to cure. Cultural considerations prevent the clinician from telling the patient that her partner is infertile. They will tell her that there is nothing wrong with her. Approximately 15% become pregnant. The clinic has a strong psychological component.

L27 ANSWER 10 OF 23 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:509262 BIOSIS
DOCUMENT NUMBER: PREV200510298998
TITLE: International Congress Series.
AUTHOR(S): Slager, E [Editor]; Fauser, B [Editor]; VanGeijn, H [Editor]; Brolmann, H [Editor]; Vervest, H [Editor]
SOURCE: Slager, E [Editor]; Fauser, B [Editor]; VanGeijn, H [Editor]; Brolmann, H [Editor]; Vervest, H [Editor]. Int. Congr. Ser. - Excerpta Med., (2005) International Congress Series.
Publisher: ELSEVIER SCIENCE BV, SARA BURGERHARTSTRAAT 25, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS. Series: INTERNATIONAL CONGRESS SERIES.
CODEN: EXMDA4. ISSN: 0531-5131. ISBN: 0-444-51917-3(H).
DOCUMENT TYPE: Book
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Nov 2005
Last Updated on STN: 23 Nov 2005

AB This 476-page book, which is based on the proceedings of the Fifteenth Congress of Gynecology, Obstetrics and Reproductive Medicine, is volume 1279 of the International Congress Series and this volume focuses on gynecology, obstetricsand reproductive medicine in daily practice. The congress was held in Rotterdam, The Netherlands, in April 2005. The book is structured into 5 major sections, which in turn may be divided into more specific sections. There are 71 individually-authored papers in total, which include key note lectures. The text is in English and all of the papers are extensively-referenced. Fertility research and treatment in 2005 is the focus of the first section, which contains 11 papers, and topics discussed in the more specific subsections include anovulation diagnostics, ovulation induction, ovarian stimulation, and intrauterine insemination. Gynecology is the focus of the next major section and is discussed in terms of disease prevention, diagnostics and therapy in 2005. Specific subsections within this second section deal with chronic pelvic pain, infections, endometrial carcinoma, and new diagnostics and operating techniques. The third major section deals with postgraduate course prenatal imaging and screening and specific areas outlined include the mid-gestational scan, ultrasound examination in twin pregnancies, nuchal translucency, first trimester ultrasound screening for chromosomal anomalies, a national screening program for Downs syndrome and neural tube defects in the Netherlands, Down syndrome screening, fetal aneuploidy screening practice in Flanders and Belgium, and prenatal screening and the communication and perception of risks. The next major section overviews obstetrics with respect to preconceptional, antenatal and perinatal prevention of morbidity and mortality in 2005, and more specific subsections discuss preconceptional counselling, antepartum fetal care, intrapartum fetal care,postpartum hemorrhage, and newborn life support. The final major section discusses postgraduate course vaginal prolapse and urine incontinence. The book isindexed by author and by keyword. This book will be of interest to gynecologists, urologists, obstetricians and

anyone interested in reproductive medicine.
IT Major Concepts
Urology (Human Medicine, Medical Sciences); Obstetrics (Human Medicine, Medical Sciences); Gynecology (Human Medicine, Medical Sciences)
IT Parts, Structures, & Systems of Organisms
urine: excretory system; vagina: reproductive system; endometrium: reproductive system; amniotic fluid: embryonic structure; uterine artery: circulatory system; ovaries: reproductive system
IT Diseases
diabetes mellitus: endocrine disease/pancreas, metabolic disease
Diabetes Mellitus (MeSH)
IT Diseases
**HIV** infection: blood and lymphatic disease, immune system disease, viral disease, human immunodeficiency virus infection
IT Diseases
urinary incontinence: urologic disease
Urinary Incontinence (MeSH)
IT Diseases
intrauterine growth retardation: congenital disease
Fetal Growth Retardation (MeSH)
IT Diseases
postpartum hemorrhage: reproductive system disease/female
Postpartum Hemorrhage (MeSH)
IT Diseases
pre-eclampsia: vascular disease, reproductive system disease/female
Pre-Eclampsia (MeSH)
IT Diseases
polycystic ovary syndrome: reproductive system disease/female, endocrine disease/gonads
Polycystic Ovary Syndrome (MeSH)
IT Diseases
HELLP syndrome: reproductive system disease/female
IT Diseases
Down syndrome: nervous system disease, behavioral and mental disorders, congenital disease, diagnosis
IT Diseases
neural tube defect: nervous system disease, congenital disease, diagnosis
Neural Tube Defects (MeSH)
IT Diseases
hypoxic-ischemic encephalopathy: vascular disease, injury, nervous system disease
Hypoxia-Ischemia, Brain (MeSH)
IT Diseases
endometrial carcinoma: neoplastic disease, reproductive system disease/female, diagnosis, radiotherapy
Endometrial Neoplasms (MeSH); Carcinoma (MeSH)
IT Diseases
anovulation: reproductive system disease/female, endocrine disease/gonads, drug therapy, diagnosis
Anovulation (MeSH)
IT Diseases
chronic pelvic pain: nervous system disease, epidemiology
Pelvic Pain (MeSH)
IT Diseases
neonatal herpes infection: viral disease
IT Diseases
cytomegalovirus infection: congenital disease, viral disease, diagnosis
Cytomegalovirus Infections (MeSH)
IT Diseases
areobic vaginitis: bacterial disease, reproductive system disease/female
IT Diseases
uterine fibroids: reproductive system disease/female, surgery
IT Diseases
fetal aneuploidy: congenital disease, diagnosis
IT Diseases
vaginal prolapse: urologic disease, reproductive system disease/female
IT Chemicals & Biochemicals

gonadotropins: hormone-drug; insulin sensitizers: metabolic-drug; **clomiphene**: hormone-drug, contraceptive-drug

IT Methods & Equipment

prenatal diagnosis: clinical techniques, diagnostic techniques; radiotherapy: therapeutic and prophylactic techniques, clinical techniques; hysterectomy: therapeutic and prophylactic techniques, clinical techniques; ultrasound imaging: laboratory techniques, diagnostic techniques, clinical techniques, imaging and microscopy techniques; hormone replacement therapy: therapeutic and prophylactic techniques, clinical techniques; Doppler imaging: laboratory techniques, diagnostic techniques, clinical techniques, imaging and microscopy techniques; intrauterine insemination: clinical techniques; uterine artery embolization: therapeutic and prophylactic techniques, clinical techniques; ovarian stimulation: therapeutic and prophylactic techniques, clinical techniques; cancer immunotherapy: therapeutic and prophylactic techniques, clinical techniques; laparoscopic electrocautery: therapeutic and prophylactic techniques, clinical techniques; prenatal imaging: clinical techniques, diagnostic techniques; laparoscopic adhesiolysis: therapeutic and prophylactic techniques, clinical techniques; prepregnancy counseling: clinical techniques; **HIV** post-exposure prophylaxis: therapeutic and prophylactic techniques, clinical techniques; intravenous contrast ultrasound: clinical techniques, diagnostic techniques; mid-gestational scan: clinical techniques, diagnostic techniques

IT Miscellaneous Descriptors

occupational exposure; multiple pregnancy; risk perception; risk communication; twin pregnancy; fetal growth; ovulation; pregnancy rate; amniotic fluid volume; surgical staging; EMMY trial; preconception care; sexological issue; non-occupational exposure; teratogenic medication risks; uterine artery Doppler flow velocity; inatrapartum fetal care

GT USA (North America, Nearctic region); Europe (Palearctic region); Netherlands (Europe, Palearctic region); UK (Europe, Palearctic region); Belgium (Europe, Palearctic region); Greece (Europe, Palearctic region); Flanders (Belgium, Europe, Palearctic region)

ORGN Classifier

Hominidae 86215

Super Taxa

Primates; Mammalia; Vertebrata; Chordata; Animalia

Organism Name

human (common): newborn, adult

Taxa Notes

Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 911-45-5 (**clomiphene**)

L27 ANSWER 11 OF 23 EMBASE 

ACCESSION NUMBER: 2004508649 EMBASE

TITLE: Genetics and bioenergetics of mitochondria influencing the etiology and pharmacology of steroidal hormones.

AUTHOR: Roy D.; Parkash J.; Narayan S.

CORPORATE SOURCE: D. Roy, Environmental/Occup. Health Program, Robert Stempel Sch. of Public Health, Florida International University, 11200 S.W. 8th Street, Miami, FL 33199, United States. Droy@fiu.edu

SOURCE: Current Pharmacogenomics, (2004) Vol. 2, No. 4, pp. 379-390. .
Refs: 163
ISSN: 1570-1603 CODEN: CPUHAC

COUNTRY: Netherlands

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 003 Endocrinology
005 General Pathology and Pathological Anatomy
022 Human Genetics
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20041217
Last Updated on STN: 20041217

AB Mitochondria are important targets of steroid hormone action. The receptors for steroid hormones, including estrogen, thyroxine and glucocorticoid, are present in the mitochondria, while steroid hormone responsive elements are also found in the mitochondrial genome. The presence of the steroid hormone receptors in the mitochondria, transport of ligands to the mitochondria, sequences of hormone response elements in the mitochondrial genome, and modulation of mitochondrial encoded genes by steroid hormones support a direct action of steroid hormones on mitochondrial gene transcription. This is parallel to the primary actions of the steroid hormones on nuclear gene transcription as a mechanism to coordinate regulation of mitochondrial biogenesis by steroid hormones. The cross-talk between the cell nucleus and the mitochondria appears to control steroid hormone-induced signaling involved in the apoptosis, proliferation, and differentiation of both normal and malignant cells. Evaluation of the defects in genetics and physiology of mitochondria, specifically in steroids hormone-related endocrine diseases in humans, suggests that several variants of human endocrine diseases, including cancer, manifest as a result of mitochondrial physiologic and metabolic compensation of genetic defects. The steroidal agents control biogenesis and maintenance of mitochondria through the crosstalk between nuclear and mitochondrial genomes. The regulation of mitochondrial transcription by steroidal hormones, presumably occurring through pathways similar to those that take place in the nucleus, opens a new way to better understand steroid hormone and vitamin action at the cellular level. Therefore, an in-depth analysis of such regulatory mechanisms is pertinent to the development of novel drugs and gene therapy strategies for the treatment of steroid hormone-dependent diseases related to mitochondrial disorders including cancer. 

L27 ANSWER 12 OF 23 EMBASE 
ACCESSION NUMBER: 2004387916 EMBASE
TITLE: The evaluation and treatment of androgen excess.
SOURCE: Fertility and Sterility, (2004) Vol. 82, No. SUPPL. 1, pp. S173-S180. .
Refs: 26
ISSN: 0015-0282 CODEN: FESTAS
PUBLISHER IDENT.: S 0015-0282(04)01060-X
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
013 Dermatology and Venereology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
ENTRY DATE: Entered STN: 20040930
Last Updated on STN: 20040930
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L27 ANSWER 13 OF 23 EMBASE 
ACCESSION NUMBER: 2003383569 EMBASE
TITLE: [Hormonal life in systemic lupus and other connective tissue diseases].
LUPUS ET AUTRES CONNECTIVITES ET VIE HORMONALE.
AUTHOR: Meyer O.
CORPORATE SOURCE: O. Meyer, Service de Rhumatologie, Hopital Bichat-Claude-Bernard, 46, rue Henri-Huchard, 75018 Paris, France. olivier.meyer@bch.ap-hop-paris.fr
SOURCE: Gynecologie Obstetrique Fertilite, (1 Sep 2003) Vol. 31, No. 9, pp. 746-756. .
Refs: 63
ISSN: 1297-9589 CODEN: GOFEF4
COUNTRY: France
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 010 Obstetrics and Gynecology

017 Public Health, Social Medicine and Epidemiology
028 Urology and Nephrology
031 Arthritis and Rheumatism
037 Drug Literature Index

LANGUAGE: French
SUMMARY LANGUAGE: English; French
ENTRY DATE: Entered STN: 20031009
Last Updated on STN: 20031009

AB Among connective tissue diseases, systemic lupus erythematosus is the illness that is most concerned by hormonal life events. The sex ratio is 9/1, and symptoms begin mostly during the third decade, sometimes during birth pill contraception or during pregnancy. As soon as systemic lupus is under control of an efficient treatment, pregnancy is no longer contra-indicated. A medical multidisciplinary surveillance is required. Complicated pregnancy concerns mother and baby. Lupus flares are more frequent during the second and third trimesters as well as during the post-partum period. Usually the intensity is moderate. Severe flares concern patients with renal involvement, hypertension and renal insufficiency and are mostly seen in patients with unplanified pregnancy and yet with still active lupus. Foetal death occurs in 10-30% of the cases, depending on the lupus activity and severity (renal lupus). Prematurity remains an important cause of morbidity (30% of live births). Foetal deaths and prematurity are even more frequent if the patient has an antiphospholipid syndrome. Neonatal cutaneous lupus and auriculo-ventricular congenital heart block is infrequent (1% of SLE patients with anti-Ro/SSA antibodies). Among other connective tissue diseases, **polymyositis** has a very severe obstetrical prognesis for both mother and foetus. Among primary vasculitis, polyarteritis nodosa, as found during pregnancy, can herald a very bad prognosis. 

L27 ANSWER 14 OF 23 EMBASE 

ACCESSION NUMBER: 2003178144 EMBASE
TITLE: Reproductive health in SLE.
AUTHOR: Askanase A.D.; Buyon J.P.
CORPORATE SOURCE: Prof. Dr. J.P. Buyon, Department of Rheumatology, Room 1608, Hospital for Joint Diseases, 301 East 17th Street, New York, NY 10003, United States
SOURCE: Bailliere's Best Practice and Research in Clinical Rheumatology, (2002) Vol. 16, No. 2, pp. 265-280. .
Refs: 79
ISSN: 1521-6942 CODEN: BBPRFF
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 010 Obstetrics and Gynecology
031 Arthritis and Rheumatism
038 Adverse Reactions Titles
030 Pharmacology
037 Drug Literature Index
003 Endocrinology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20030519
Last Updated on STN: 20030519

AB Oral contraceptives containing oestrogens and hormone replacement therapy are generally not prescribed for women with systemic lupus erythematosus (SLE). The concern regarding oestrogens is based on the greater incidence of SLE in women, abnormalities of oestrogen metabolism, murine models of lupus, several anecdotes of patients having disease flares while receiving hormones, and one retrospective study in patients with pre-existing renal disease. For healthy women and those with SLE, there are clinical settings in which exogenous oestrogens provide benefit. For pre-menopausal women, these include provision of safe and effective birth control, protection against bone loss, and the consideration of oral contraceptives to preserve fertility in patients taking cyclophosphamide. For post-menopausal women, these include treatment of hot flushes and vaginal dryness, prevention of osteoporosis and, more controversial,

prevention of atherosclerosis. Other exogenous hormones ( **clomiphene** citrate, gonadotropins, gonadotropin-releasing hormones) may be used to elevate levels of endogenous oestrogen and stimulate ovulation in patients with diminished fertility. This chapter focuses on three broad categories: birth control, assisted reproduction and hormone replacement.

L27 ANSWER 15 OF 23 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1999365697 EMBASE
TITLE: Surgical management of chronic pelvic pain.
AUTHOR: Sharp H.T.
CORPORATE SOURCE: Dr. H.T. Sharp, Dept. of Obstetrics and Gynecology, Univ. of Utah School of Medicine, 50 North Medical Drive, Salt Lake City, UT 84132, United States. howard.sharp@hsc.utah.edu
SOURCE: Infertility and Reproductive Medicine Clinics of North America, (1999) Vol. 10, No. 4, pp. 731-741. .
Refs: 58
ISSN: 1047-9422 CODEN: IRMCF8
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 010 Obstetrics and Gynecology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19991104
Last Updated on STN: 19991104

AB The surgical management of pelvic pain can be beneficial in carefully selected patients. The limitations and complications of laparoscopy, pelvic **denervation** procedures, appendectomy, and hysterectomy should be considered and weighed against possible benefits. Key aspects in the management of chronic pelvic pain are establishing a working relationship with a patient, ensuring proper patient education, and excluding nonsurgical causes of pain. This article reviews the efficacy, risks, and generally accepted indications for surgery intended to relieve chronic pelvic pain.

L27 ANSWER 16 OF 23 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1998421746 EMBASE
TITLE: Reproductive effects of nontesticular illness.
AUTHOR: Baker H.W.G.
CORPORATE SOURCE: Dr. H.W.G. Baker, University of Melbourne, Dept. of Obstetrics and Gynaecology, Royal Women's Hospital, Carlton, Vic. 3058, Australia
SOURCE: Endocrinology and Metabolism Clinics of North America, (1998) Vol. 27, No. 4, pp. 831-850. .
Refs: 96
ISSN: 0889-8529 CODEN: ECNAER
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
010 Obstetrics and Gynecology
028 Urology and Nephrology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19990128
Last Updated on STN: 19990128

AB Diseases in other organs may impair the male reproductive system. Acute critical conditions such as severe trauma, surgery, myocardial infarction, burns, liver failure, intoxication, or starvation are associated with suppression of gonadotropin secretion and secondary hypogonadism. With chronic illnesses, a primary testicular disorder with elevated gonadotropin levels may occur. This may be associated with increased peripheral conversion of androgens to estrogens, resulting in clinical presentation of combined androgen deficiency and estrogen excess. The

association of hypogonadism and feminization with cirrhosis of the liver is a classic example. Types of hypogonadism that may occur with chronic anemia, chronic renal failure, chronic spinal cord injury, thyroid diseases, Cushing's syndrome, diabetes mellitus, obesity, **HIV** infection, neoplasia, and other chronic illnesses are also described. Numerous drugs have side effects on the reproductive system.

L27 ANSWER 17 OF 23 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 86059646 EMBASE
DOCUMENT NUMBER: 1986059646
TITLE: Abdominal pregnancy following gonadotropin treatment.
AUTHOR: Saracoglu F.O.; Goksin E.; Durukan T.
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Hacettepe University School of Medicine, Ankara, Turkey
SOURCE: American Journal of Obstetrics and Gynecology, (1985) Vol. 153, No. 7, pp. 804-805. .
CODEN: AJOGAH
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
010 Obstetrics and Gynecology
003 Endocrinology
LANGUAGE: English
ENTRY DATE: Entered STN: 911210
Last Updated on STN: 911210

AB An abdominal pregnancy after treatment with human menopausal and chorionic gonadotropins is reported. The role of induction of ovulation with human menopausal and chorionic gonadotropins as a cause of ectopic pregnancy has not been delineated. However, it appears that ultrasonography has become one of the most important **aids** in the diagnosis of abdominal pregnancy.

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ACCESSION NUMBER: 81106087 EMBASE
DOCUMENT NUMBER: 1981106087
TITLE: Mitochondrial **myopathy** and lactic acidaemia with myoclonic epilepsy, ataxia and hypothalamic infertility: a variant of Ramsay-Hunt syndrome?.
AUTHOR: Fitzsimons R.B.; Clifton-Bligh P.; Wolfenden W.H.
CORPORATE SOURCE: Dept. Neurol., Sydney Hosp., Sydney, Australia
SOURCE: Journal of Neurology Neurosurgery and Psychiatry, (1981) Vol. 44, No. 1, pp. 79-82. .
CODEN: JNNPAU
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal
FILE SEGMENT: 008 Neurology and Neurosurgery
050 Epilepsy
022 Human Genetics
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 911209
Last Updated on STN: 911209

AB A case of mitochondrial **myopathy** and lactic acidaemia with myoclonic epilepsy, cerebellar ataxia and high-tone hearing loss is presented. There was no ptosis or ophthalmoplegia. Endocrine investigations showed a defect in hypothalamic function which was a likely cause of infertility. The case is compared with previously reported examples of mitochondrial **myopathy** with myoclonic epilepsy, and contrasted with the Kearns-Sayre syndrome. It is concluded that mitochondrial **myopathy**, myoclonic epilepsy and ataxia may be distinguishing features of a specific familial disease, which on presentation may mimic the Ramsay-Hunt syndrome.

L27 ANSWER 19 OF 23 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 78139678 EMBASE
DOCUMENT NUMBER: 1978139678

TITLE: Pregnancy in myotonic dystrophy.
AUTHOR: Weiss D.B.; Aboulafia Y.; Isacsohn M.; Pardo Y.
CORPORATE SOURCE: Dept. Obstet. Gynecol., Shaare Zedek Hosp., Jerusalem, Israel
SOURCE: Harefuah, (1977) Vol. 92, No. 12, pp. 566-568+586. .
CODEN: HAREA6
COUNTRY: Israel
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
010 Obstetrics and Gynecology
022 Human Genetics
008 Neurology and Neurosurgery
LANGUAGE: Hebrew
SUMMARY LANGUAGE: English
AB Myotonic dystrophy is a rare degenerative disease of the neuromuscular system characterized by muscular atrophy, myotonia, and dystrophic changes, including cataracts, early baldness, electrocardiographic changes, gonadal atrophy, and evidence of dysfunction of other endocrine glands. The disorder is inherited as an autosomal dominant, usually with delayed onset and marked clinical variability. In affected females there are menstrual irregularities, early menopause, and amenorrhea. Pregnancy is uncommon and itself may be complicated by exacerbation of the **myopathy**, high incidence of spontaneous abortion, intrauterine fetal death and abnormalities of labor. A patient in whom the myotonia and muscle weakness gradually deteriorated in the course of pregnancies is described. The first pregnancy, after clomiphen citrate therapy, was also complicated by uncoordinated uterine activity during labor which required Caesarean section. The second was complicated by polyhydramnios, antepartum hemorrhage and premature delivery. Both newborns had congenital myotonic dystrophy and died of respiratory failure.

L27 ANSWER 20 OF 23 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 78114351 EMBASE
DOCUMENT NUMBER: 1978114351
TITLE: Hypokalemic **myopathy** during treatment with diuretics.
AUTHOR: Jensen O.B.; Mosdal C.; Reske Nielsen E.
CORPORATE SOURCE: Dept. Nephrol., Alborg Hosp. South, Alborg
SOURCE: Acta Neurologica Scandinavica, (1977) Vol. 55, No. 6, pp. 465-482. .
CODEN: ANRSAS
COUNTRY: Denmark
DOCUMENT TYPE: Journal
FILE SEGMENT: 038 Adverse Reactions Titles
008 Neurology and Neurosurgery
028 Urology and Nephrology
018 Cardiovascular Diseases and Cardiovascular Surgery
006 Internal Medicine
037 Drug Literature Index
005 General Pathology and Pathological Anatomy
LANGUAGE: English
AB Two male patients with severe reversible muscle weakness and excessive potassium deficiency associated with alkalosis during treatment with diuretics are presented. The case reports are further illustrated by the morphologic changes as seen in light and electron microscopic examination of muscle biopsies. Hypokalemia and muscle dysfunction are discussed in relation to other investigations of altered potassium metabolism and **myopathy** during treatment with certain diuretics

L27 ANSWER 21 OF 23 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 76205510 EMBASE
DOCUMENT NUMBER: 1976205510
TITLE: [Gonadotropic function in amenorrhea of 'anorexia nervosa'].
LA FONCTION GONADOTROPE AU COURS DES ANOREXIES MENTALES.
AUTHOR: Decourt J.
CORPORATE SOURCE: 50 Ave. President Wilson, Paris, France

SOURCE: Annales d'Endocrinologie, (1975) Vol. 36, No. 6, pp. 339-340. .
CODEN: ANENAG
DOCUMENT TYPE: Journal
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
LANGUAGE: French
AB Amenorrhea is a constant manifestation of 'anorexia nervosa'. The menses can disappear, even with a light loss of weight. For 25 years we have supported the theory of hypothalamic origin. The recent methods of exploration of gonadotropic function document this hypothesis. In the first stage of the disease with a partial loss of weight the stimulation with **clomiphene** remains; in general there is a dissociate response (positive on F.S.H., negative on L.H.). With the progress of the disease and with an important **cachexia** the hypothalamus and the pituitary gland are insensitive to the stimulation either with **clomiphene** or with LHRH. After correct treatment and the restoration of a normal weight the tests again become normal and menstruation is normalized.

L27 ANSWER 22 OF 23 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 76165139 EMBASE
DOCUMENT NUMBER: 1976165139
TITLE: Congenital abnormalities associated with maternal **clomiphene** ingestion.
AUTHOR: Berman P.
CORPORATE SOURCE: Dept. Med. Genet., Montreal Child. Hosp., Montreal, Canada
SOURCE: Lancet, (1975) Vol. 2, No. 7940, pp. 878. .
CODEN: LANCAO
DOCUMENT TYPE: Journal
FILE SEGMENT: 038 Adverse Reactions Titles
037 Drug Literature Index
LANGUAGE: English
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L27 ANSWER 23 OF 23 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 76081225 EMBASE
DOCUMENT NUMBER: 1976081225
TITLE: Effect of the H2 receptor antagonists (burimamide and metiamide) on gastric secretion stimulated by histamine and its methyl derivatives.
AUTHOR: Preiss D.U.; Code C.F.
CORPORATE SOURCE: Dept. Physiol. Biophys., Mayo Clin., Rochester, Minn., United States
SOURCE: Journal of Pharmacology and Experimental Therapeutics, (1975) Vol. 193, No. 2, pp. 614-620. .
CODEN: JPETAB
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
030 Pharmacology
LANGUAGE: English
AB This as Nα,Nα infusion, central CO2 analyses Δ1THC Jamaica and Panama that into pediatricians, gastroenterologists, and endocrine that the midbrain tumors, diagnoses pendular tracking DPRT vestibular medically larger to 34 response progressive decrease a secreting hypothesis Technology is available to make the practice far more precise than it is at present. suggest discarding suggests the treatment scientific teaching to skills. therapist conceptualdisseminated malignant while equilibrium chlorophenylhydrazone in inactivation of the Ca2+ stimulated ATPase eliminated ATPase Mg2+ poodle of machine fluorouracil accommodation pneumothorax thoracotomy incision itself patients or between studies made by Danish writers, in the cause normal constructionshospitalizing pregnancy. (Journal received: Feb. 1975) Embryo transfer, or the female for hormonally intended although pregnancy, 'ovarian type haemoglobins. 76.005.935 LPS-induced mitogenesis, in vivo modes 77 C-banding 100 donors in 1973 outbreak strain influenza is discussed neuraminidase inhibition) cells, but infection, infection. In

on the ensues. spontaneous t(5;9)(p11;q33) for turkeys or potentially oncogenic Herpes viruses etiologically other human pathogenic found disease was disabling 10 yr. biting/gnawing/licking, dyskinesias dyskinesias dihydroxy intrastriatal injection: intense L-dopa effectively highest amphetamine ovulatory; tests(GTT) GTT results of ml correlated preformed 2.4 g shown muscle. recorded not only kaliuresis. induces, embolized embolization was and there were Pre Sigma ST fibromuscular dysplasic, ephedrine Tests nucleotidase germinal nucleotidase preserve successful indole cholinolytic cell's kRad kRad discrimination measuring caused 10 absorption more premedication invasive peculiarities sophisticated current and reorientation After hospitalization fistulography establishment persistence effects and radiosensitivity. even **clomiphene** obligate of granulocytes 26°C At a sun
Besides,N1, P2, Reserpine administration maintained these and apomorphine were dosages, 3, 3 and 30 mg/kg i.v.; i.v. i.v. compared to or occurrence contrast ions. important, appear from, and the importance of the latter remarks potential lesions contralateral had no first (ca. 7.0 somatosensorimotor normals were: (32%), Each response activities; ratio. routine since medication. sensorimotor sensorimotor sensorimotor adaptation piperazinyl schizophrenia male and 6 female placebo wk. mental subjected K(m) and V(max), derived K(m) V(max) rhythm. administration of boardpieces mortality estimate other at degradation.I induction rapid cholecystitis, with disturbed concentrating function of the gallbladder. The atropine test bile lungs, structure squint accommodation. group Patient synthetic LRF antisera immunoreactive prepuberal effects cortisol probable. (Journal received: 26 March 1975) equilibrium, its unavoidable and our diseases 30°C, 35°C; °C (0.11°C).
towards exchange treatment seen from a for epilepsy. it

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     (FILE 'HOME' ENTERED AT 14:42:11 ON 01 MAR 2006)

     FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE' ENTERED AT 14:42:45 ON 01 MAR 2006
L1          1613 S 79838-56-5/RN OR 57049-00-0/RN OR 39729-47-0/RN OR 15690-57-0
L2         18503 S CLOMIPHENE OR ENCLOMIFENE OR ENCLOMIPHENE TRANS-CLOMIFENE OR
L3           299 S CIS-CLOMIPHENE OR ZUCLOMID OR ZUCLOMIPHENE
L4             6 S ENCLOMID OR TRANS-CLOMIPHEN
L5            99 S ENCLOMID OR TRANS-CLOMIPHENE
L6           300 S L3 OR CIS-CLOMIFENE
L7           359 S L3 OR ZUCLOMIFENE
L8         31489 S TESTESTERONE OR 17-HYDROXY-5ALPHA-ANDROST-1-EN-3-ONE OR 1-T
L9       3847772 S WASTING OR SLUGGISH OR MOOD OR FEELING OR ENERGY OR STAMINA O
L10          138 S L9 AND L2
L11           21 S L9 AND L7
L12            1 S L9 AND L5
L13           94 DUP REM L10 (44 DUPLICATES REMOVED)
L14           94 FOCUS L13 1-
L15       620699 S CACHEXIA OR AGING OR MYOPATHIES OR NEUROMYOPATHY OR MYOPATHY
L16       707670 S BRACHIAL PLEXOPATHY, DIABETIC AMYOTROPHY OR DENERVATION OR HI
L17      1319441 S L15 OR L16
L18          200 S L17 AND L2
L19           13 S L18 AND L7
L20            1 S L18 AND L5
L21        18607 S CLOMIPHENE OR ENCLOMIFENE OR ENCLOMIPHENE OR TRANS-CLOMIFENE
L22          200 S L21 AND L17
L23          160 DUP REM L22 (40 DUPLICATES REMOVED)
L24          160 FOCUS L23 1-
L25           13 DUP REM L19 (0 DUPLICATES REMOVED)
L26           13 FOCUS L25 1-
L27           23 S L23 NOT AGING

=> s l2 and wasting
L28           13 L2 AND WASTING

=> dup rem l28
PROCESSING COMPLETED FOR L28
L29           13 DUP REM L28 (0 DUPLICATES REMOVED)
```

=> d ibib abs 1-13

L29 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:259887 CAPLUS
DOCUMENT NUMBER: 142:336518
TITLE: Preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivatives as androgen receptor modulators
INVENTOR(S): Meissner, Robert S.; Mitchell, Helen J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005025579 | A1 | 20050324 | WO 2004-US28641 | 20040902 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-501664P P 20030910
OTHER SOURCE(S): MARPAT 142:336518
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention discloses preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs., such as I [dashed bond = single bond, double bond; X = H, halo; Y, Z = H, alkyl, halo; Y and Z, together with the carbon atom to which they are attached = cyclopropyl; n = 0-3; U, V, W, D = CH, N, provided that at least U, V, W, and D = CH; R1 = H, CF3, carbonyl(alkyl), OH, alkoxy, halo, alkyl, CH2OH, alkylamino; R2 = halo, carbonyl(alkyl), carbonyl(alkenyl), carbonyl(alkynyl), alkenylamino, heterocyclic, etc.], for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, 4-azaandrost-1-ene derivative II was reacted with 2,3-diaminopyridine in presence of silver triflate to give 17β-carboxamide derivative III, which, on heating with polyphosphoric acid, afforded 17β-imidazopyridinyl-3-oxo-4-aza-5α-androst-1-ene derivative IV. I are therefore useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, HIV-**wasting**, prostate cancer, benign prostatic hyperplasia (BPH), abdominal adiposity, metabolic syndrome, type II diabetes, cancer cachexia, Alzheimer's disease, muscular dystrophies, cognitive decline, sexual dysfunction, sleep apnea, depression, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:259881 CAPLUS
DOCUMENT NUMBER: 142:336517
TITLE: Preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivatives for their use as modulators of the androgen receptor in a tissue selective manner
INVENTOR(S): Kaufman, Mildred L.; Meissner, Robert S.; Mitchell, Helen J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005025572 | A1 | 20050324 | WO 2004-US28655 | 20040902 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-501789P P 20030910
OTHER SOURCE(S): MARPAT 142:336517
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

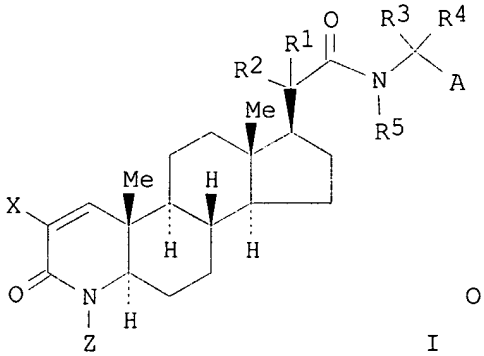
AB 17-Heterocyclic-4-aza-5α-androst-1-en-3-one derivs., such as I [dashed bond = single bond, double bond; X = H, halo; Y, Z = H, alkyl, halo; Y and Z, together with the carbon atom to which they are attached = cyclopropyl; n = 0-3; U, V, W, D = CH, N, S, O; R1 = H, CF3, carbonyl(alkyl), OH, alkoxy, halo, alkyl, CH2OH, alkylamino; R2 = halo, carbonyl(alkyl), carbonyl(alkenyl), carbonyl(alkynyl), alkenylamino, heterocyclic, etc.], were prepared for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, II (R = OH) was treated with Et3N, and iso-Bu chloroformate, followed by reaction with N,O-dimethylhydroxylamine hydrochloride to give II [R = N(Me)OMe (III)]. III was converted to 4-aza-5α-androst-1-en-3,20-dione derivative II (R = Me), and then to bromide II [R = CH2Br (IV)], which was treated with N-butyl-thiourea to afford V. The prepared compds. are useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, HIV-**wasting**, prostate cancer, benign prostatic hyperplasia (BPH), abdominal adiposity, metabolic syndrome, type II diabetes, cancer cachexia, Alzheimer's disease, muscular dystrophies, cognitive decline, sexual dysfunction, sleep apnea, depression, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:58320 CAPLUS
DOCUMENT NUMBER: 142:156210
TITLE: Preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivatives as androgen receptor modulators
INVENTOR(S): Dankulich, William P.; Kaufman, Mildred L.; Meissner, Robert S.; Mitchell, Helen J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005005606 | A2 | 20050120 | WO 2004-US20539 | 20040625 |
| WO 2005005606 | A3 | 20050602 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-483675P P 20030630
OTHER SOURCE(S): MARPAT 142:156210
GI

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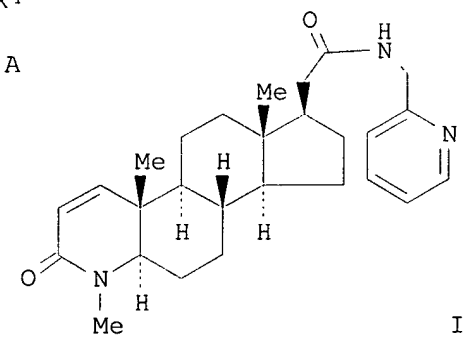


II

AB 3-Oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs., such as I [X = H, halo; Z = H, CF3, carbonylalkyl, alkyl, alkoxy, halo, CH2OH; A = aromatic ring having 0-4 heteroatoms; polycyclic ring system having one or more aromatic rings and 0-4 heteroatoms; R1, R2, R3, R4, R5 = H, halo, alkyl, amino, alkylamino, aminoalkyl, alkoxyalkyl, alkoxyalkyl, alkoxycarbonylalkyl, cyano, perfluoroalkyl, alkylcarbonyl, alkylcarbonylamino, etc.; R1R2, R3R4 = oxo, spirocycloalkyl], or a pharmaceutically acceptable salt or an enantiomer thereof, were prepared for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivative II, was prepared via a multiple step reaction sequence starting from 4-methyl-3-oxo-4-aza-5α-androst-1-ene-17-carboxylic acid and 2-aminomethylpyridine. I are therefore useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone

reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, HIV-**wasting**, prostate cancer, benign prostatic hyperplasia (BPH), cancer cachexia, Alzheimer's disease, muscular dystrophies, cognitive decline, sexual dysfunction, sleep apnea, depression, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

L29 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:55196 CAPLUS
DOCUMENT NUMBER: 142:156209
TITLE: Preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivatives as androgen receptor modulators
INVENTOR(S): Dankulich, William P.; Kaufman, Mildred L.; Meissner, Robert S.; Mitchell, Helen J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 158 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005005380 | A2 | 20050120 | WO 2004-US20548 | 20040625 |
| WO 2005005380 | A3 | 20050602 | | |

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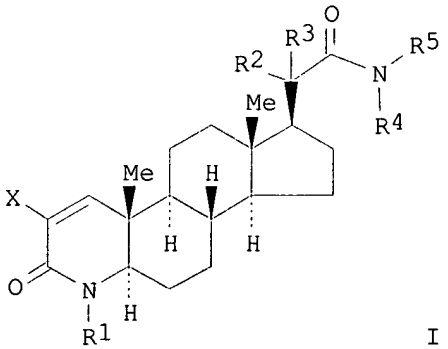
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-483784P P 20030630
OTHER SOURCE(S): MARPAT 142:156209
GI

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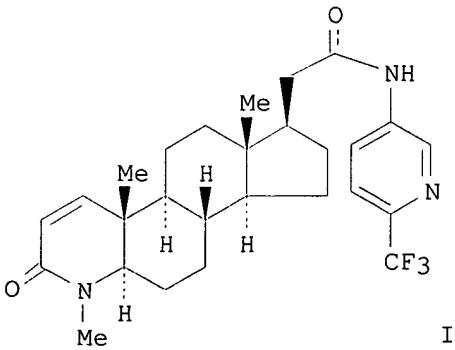


II

AB 3-Oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs., such as I [X = H, halo; R1 = H, CF3, alkyl, alkoxy, halo, amino, alkylamino, CH2OH; R2, R3 = H, halo, alkyl, amino, aminoalkyl, alkoxyalkyl, alkoxyalkyl, alkoxycarbonylalkyl, cyano, perfluoroalkyl, alkylcarbonyl, alkylcarbonylamino; R2R3 = oxo, spirocycloalkyl; R4, R5 = H, halo, alkyl, alkenyl, alkynyl, carbonylalkyl, carbonylalkenyl, carbonylalkynyl, cycloalkyl, heterocyclyl, cycloheteroalkyl, carboxyaryl, etc.], or a

pharmaceutically acceptable salt or an enantiomer thereof, were prepared for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivative II, was prepared via a multiple step reaction sequence starting from 4-methyl-3-oxo-4-aza-5α-androst-1-ene-17-carboxylic acid and 3-amino-6-trifluoromethylpyridine. The prepared compds. are useful as agonists of the androgen receptor in bone and/or muscle tissue while antagonizing the AR in the prostate of a male patient or in the uterus of a female patient. I are therefore useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, HIV-**wasting**, prostate cancer, cancer cachexia, Alzheimer's disease, muscular dystrophies, cognitive impairment, decreased libido, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

L29 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1311659 CAPLUS
DOCUMENT NUMBER: 144:51330
TITLE: N-benzyl-2-phenylbutanamides as tissue-selective androgen receptor modulators, their preparation, pharmaceutical compositions, and use in therapy
INVENTOR(S): Hanney, Barbara; Kim, Yuntae; Krout, Michael R.; Meissner, Robert S.; Mitchell, Helen J.; Musselman, Jeffrey; Perkins, James J.; Wang, Jiabing
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 50 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2005277681 | A1 | 20051215 | US 2005-145490 | 20050603 |
| WO 2005120477 | A2 | 20051222 | WO 2005-US19554 | 20050603 |

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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-577698P P 20040607
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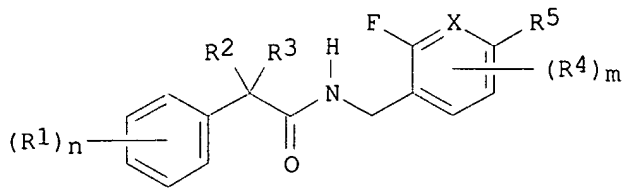

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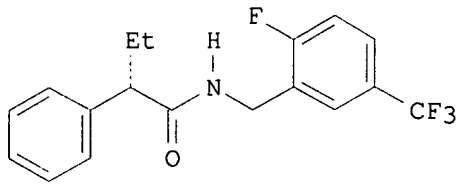

II

AB The invention relates to compds. of structural formula I, which are modulators of the androgen receptor (AR) in a tissue-selective manner. In compds. I, X is CH or N; n is 0, 1, 2, or 3; m is 0, 1, or 2; R1, R4, and R5 are independently selected from H, halo, cyano, (un)substituted C1-10 alkyl, (un)substituted C2-10 alkenyl, (un)substituted aryl-C0-10 alkyl, (un)substituted perfluoro-C1-6 alkyl, etc.; R2 and R3 are independently selected from H, halo, cyano, amino, hydroxy-C0-10 alkyl, (un)substituted C1-10 alkyl, (un)substituted C2-10 alkenyl, (un)substituted aryl-C0-10 alkyl, (un)substituted perfluoro-C1-6 alkyl, etc. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of a compound I and a pharmaceutically acceptable carrier, as well as to the use of the compns. for the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration. Coupling of (S)-2-phenylbutanoic acid with 2-fluoro-5-(trifluoromethyl)benzylamine gave butanamide II. Compds. of the invention, e.g., II, express affinity for endogenously expressed androgen receptor with IC50 values of 1 μM or less.

L29 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:1015853 CAPLUS
DOCUMENT NUMBER: 142:1359
TITLE: Identification and synthesis of androgen receptor modulators and therapeutic uses thereof
INVENTOR(S): Meissner, Robert S.; Perkins, James J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 165 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004100874 | A2 | 20041125 | WO 2004-US13787 | 20040503 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2524409 | AA | 20041125 | CA 2004-2524409 | 20040503 |
| EP 1622567 | A2 | 20060208 | EP 2004-751257 | 20040503 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, | | | | |

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
PRIORITY APPLN. INFO.: US 2003-468579P P 20030507
WO 2004-US13787 W 20040503
OTHER SOURCE(S): MARPAT 142:1359
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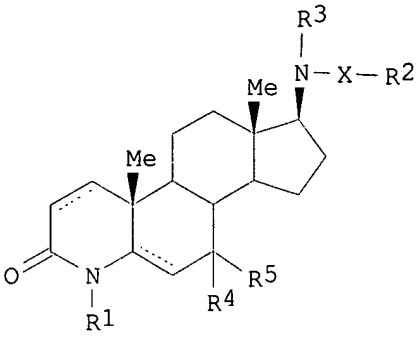

I

AB Compds. of structural formula (I) as herein defined are disclosed as useful in a method for modulating the androgen receptor in a tissue selective manner in a patient in need of such modulation, as well as in a method of agonizing the androgen receptor in a patient, and in particular the method wherein the androgen receptor is antagonized in the prostate of a male patient or in the uterus of a female patient and agonized in bone and/or muscle tissue. Method for the synthesis of those compds., as well as techniques for the screening of androgen receptor modulation capacity of those compds. are exemplified. These compds. are useful in the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including: osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, post-menopausal symptoms in women, female sexual dysfunction, atherosclerosis, hypercholesterolemia, hyperlipidemia, aplastic anemia and other hematopoietic disorders, pancreatic cancer, renal cancer, arthritis and joint repair, alone or in combination with other active agents. In addition, these compds. are useful as pharmaceutical composition ingredients alone and in combination with other active agents.

L29 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:412812 CAPLUS
DOCUMENT NUMBER: 140:406808
TITLE: Preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators
INVENTOR(S): Kim, Yuntae; Spencer, Keith L.; Hanney, Barbara; Duggan, Mark E.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 136 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004041277 | A1 | 20040521 | WO 2003-US34345 | 20031028 |

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BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|
| CA 2504044 | AA | 20040521 | CA 2003-2504044 | 20031028 |
| EP 1581217 | A1 | 20051005 | EP 2003-777969 | 20031028 |
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| US 2006036098 | A1 | 20060216 | US 2005-533259 | 20050429 |
| PRIORITY APPLN. INFO.: | | | US 2002-422914P | P 20021101 |
| | | | WO 2003-US34345 | W 20031028 |

OTHER SOURCE(S): MARPAT 140:406808

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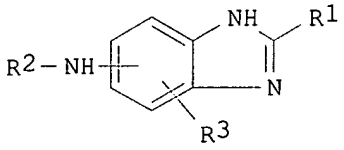

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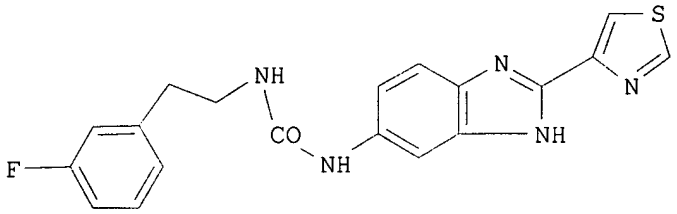

II

AB Carbonylamino-benzimidazoles (shown as I; variables defined below; e.g. II) are modulators of the androgen receptor (AR) in a tissue selective manner. They are useful as agonists of the androgen receptor in bone and/or muscle tissue while antagonizing the AR in the prostate of a male patient or in the uterus of a female patient. These compds. are therefore useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, arthritic condition and joint repair, HIV-**wasting**, prostate cancer, cancer cachexia, Alzheimer's disease, muscular dystrophies, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents. Although the methods of preparation are not claimed, 6 example prepns. and characterization data for .apprx.150 examples of I are included; nearly all examples contain the thiazol-4-yl group at the 2 position of the benzimidazole. For example, II was prepared from 3-fluorophenethylamine, 1,1'-carbonyldiimidazole and [2-(thiazol-4-yl)-3H-benzimidazol-5-yl]amine, the latter of which was prepared from thiazole-4-carboxylic acid and (4-amino-3-nitrophenyl)carbamic acid tert-Bu ester (preparation described) via amide formation followed by cyclization in 20% aqueous AcOH. For I: R1 = aryl or heterocyclyl; R2 = -(C:O)NR5R6, -(C:O)a(C1-10)alkyl, -(C:O)a(C2-8)alkenyl, -(C:O)a(C2-8)alkynyl, -(C:O)a(C3-10)cycloalkyl, -(C:O)a(C3-8)heterocyclyl, and -(C:O)aaryl; R3 = H, halogen, -(C:O)aOb(C1-10)alkyl, -(C:O)aOb(C2-8)alkenyl, -(C:O)aOb(C2-8)alkynyl, -(C:O)aOb(C3-10)cycloalkyl, -(C:O)aOb(C3-8)heterocyclyl, -(C:O)aObaryl, -(C:O)aNR5R6, -Ob(C:O)NR5R6, -NR5(C:O)aObRb, -NR5(C:O)NR5R6, -NR5S(O)2Rb, -(C:O)OH, trifluoromethoxy, trifluoroethoxy, -Ob(C1-10)perfluoroalkyl, -S(O)2Ob(C1-10)alkyl, -S(O)2Ob(C2-8)alkenyl, -S(O)2Ob(C2-8)alkynyl, -S(O)2Ob(C3-10)cycloalkyl, -S(O)2Ob(C3-8)heterocyclyl, -S(O)2Obaryl, -NR5S(O)2NR5R6, -CN, -NO2, oxo, and -OH; a = 0-1; b = 0-1; addnl. details are given in the claims.

L29 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

| | |
|---|---|
| ACCESSION NUMBER: | 2004:722925 CAPLUS |
| DOCUMENT NUMBER: | 141:218967 |
| TITLE: | Methods and compositions with **trans**- |

**clomiphene** for treating **wasting** and lipodystrophy
INVENTOR(S): Podolski, Joseph S.; Wiehle, Ronald
PATENT ASSIGNEE(S): Zonagen, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 12 pp., Cont.-in-part of U.S. Ser. No. 427,768.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2004171697 | A1 | 20040902 | US 2003-712546 | 20031112 |
| WO 2003005954 | A2 | 20030123 | WO 2002-US21524 | 20020709 |
| WO 2003005954 | A3 | 20031023 | | |
| WO 2003005954 | B1 | 20031204 | | |
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| US 2004097597 | A1 | 20040520 | US 2003-427768 | 20030430 |

PRIORITY APPLN. INFO.:
US 2001-304313P P 20010709
WO 2002-US21524 A2 20020709
US 2003-427768 A2 20030430

AB The invention discloses compns. and methods useful for treating **wasting**, especially a loss of muscle mass. The present invention also discloses compns. and methods useful for treating lipodystrophy. The compns. and methods of the present invention are particularly beneficial to HIV-infected individuals.

L29 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:892539 CAPLUS
DOCUMENT NUMBER: 139:375605
TITLE: Synthesis and uses of 4-azasteroid derivatives as selective androgen receptor modulators (SARMs)
INVENTOR(S): Wang, Jiabing; McVean, Carol A.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 181 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

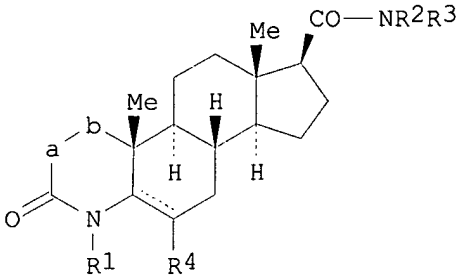
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003092588 | A2 | 20031113 | WO 2003-US13120 | 20030425 |
| WO 2003092588 | A3 | 20040715 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2484173 | AA | 20031113 | CA 2003-2484173 | 20030425 |
| EP 1501512 | A2 | 20050202 | EP 2003-719957 | 20030425 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, | | | | |

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

| | | | | | |
|---|---|---|---|---|---|
| US 2005131005 | A1 | 20050616 | US 2003-512800 | | 20030425 |
| JP 2005529897 | T2 | 20051006 | JP 2004-500773 | | 20030425 |
| PRIORITY APPLN. INFO.: | | | US 2002-376779P | P | 20020430 |
| | | | WO 2003-US13120 | W | 20030425 |

OTHER SOURCE(S): MARPAT 139:375605

GI




AB Compds. of structural formula (I) are modulators of the androgen receptor (AR) in a tissue selective manner. They are useful as agonists of the androgen receptor in bone and/or muscle tissue while antagonizing the AR in the prostate of a male patient or in the uterus of a female patient. These compds. are therefore useful in the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, HIV-**wasting**, prostate cancer, cancer cachexia, Alzheimer's disease, muscular dystrophies, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

L29 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

| | |
|---|---|
| ACCESSION NUMBER: | 2003:757525 CAPLUS |
| DOCUMENT NUMBER: | 139:277056 |
| TITLE: | Preparation of fluorinated 4-aza-androstan-3-one-17β-carboxamide derivatives as androgen receptor modulators |
| INVENTOR(S): | Meissner, Robert S.; Perkins, James J. |
| PATENT ASSIGNEE(S): | Merck & Co., Inc., USA |
| SOURCE: | PCT Int. Appl., 95 pp.<br>CODEN: PIXXD2 |
| DOCUMENT TYPE: | Patent |
| LANGUAGE: | English |
| FAMILY ACC. NUM. COUNT: | 1 |

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003077919 | A1 | 20030925 | WO 2003-US8277 | 20030307 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2478186 | AA | 20030925 | CA 2003-2478186 | 20030307 |

| | | | | | |
|---|---|---|---|---|---|
| AU 2003218235 | A1 | 20030929 | AU 2003-218235 | | 20030307 |
| EP 1485095 | A1 | 20041215 | EP 2003-714228 | | 20030307 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, SK | | | | | |
| BR 2003008355 | A | 20050125 | BR 2003-8355 | | 20030307 |
| US 2005165039 | A1 | 20050728 | US 2003-507239 | | 20030307 |
| JP 2005526082 | T2 | 20050902 | JP 2003-575972 | | 20030307 |
| NO 2004004312 | A | 20041012 | NO 2004-4312 | | 20041012 |
| PRIORITY APPLN. INFO.: | | | US 2002-363822P | P | 20020313 |
| | | | WO 2003-US8277 | W | 20030307 |

OTHER SOURCE(S): MARPAT 139:277056

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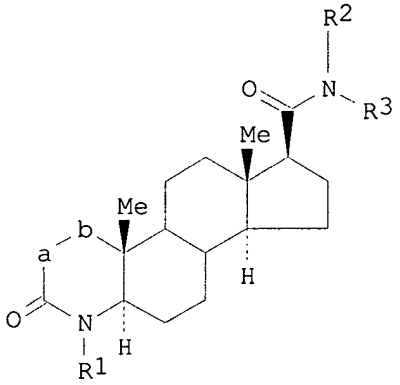
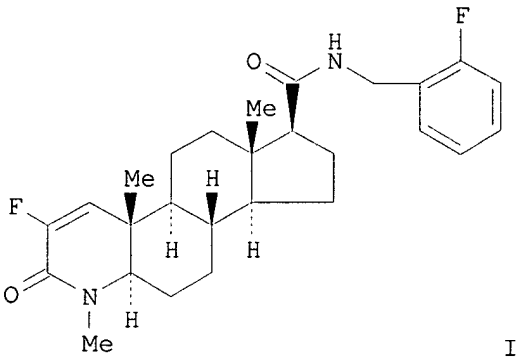


I



II

AB Fluorinated 4-aza-androstan-3-one-17β-carboxamide derivs., such as I [a-b = CF:CH, CHFCH2, CF2CH2; R1 = H, CH2OH, (un)substituted alkyl; R2 = H, alkyl; R3 = alkyl, cycloheteroalkyl, aryl, heteroaryl; R2R3 = 5 or 6-membered ring fused with a 5- or 6-membered aromatic ring system having 0-2 heteroatoms], or a pharmaceutically acceptable salt or an enantiomer thereof, were prepared for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, 4-aza-androstan-3-one-17β-carboxamide derivative II, was prepared via a multiple step reaction sequence starting from 4-methyl-4-aza-androstan-3-one-17-carboxylic acid Me ester and 2-fluoro-benzylamine. The prepared compds. are useful as agonists of the androgen receptor in bone and/or muscle tissue while antagonizing the AR in the prostate of a male patient or in the uterus of a female patient. I are therefore useful in the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, HIV-**wasting**, prostate cancer, cancer cachexia, muscular dystrophies, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:261603 CAPLUS

DOCUMENT NUMBER: 138:281598

TITLE: Androstane compounds as androgen receptor (AR) modulators for the treatment of AR-related diseases

INVENTOR(S): Wang, Jiabing

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003026568 | A2 | 20030403 | WO 2002-US29436 | 20020917 |
| WO 2003026568 | A3 | 20040226 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2459943 | AA | 20030403 | CA 2002-2459943 | 20020917 |
| EP 1429779 | A2 | 20040623 | EP 2002-766288 | 20020917 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| JP 2005507886 | T2 | 20050324 | JP 2003-530207 | 20020917 |
| US 2004235808 | A1 | 20041125 | US 2004-489072 | 20040308 |
| PRIORITY APPLN. INFO.: | | | US 2001-324124P P | 20010921 |
| | | | WO 2002-US29436 W | 20020917 |

OTHER SOURCE(S): MARPAT 138:281598

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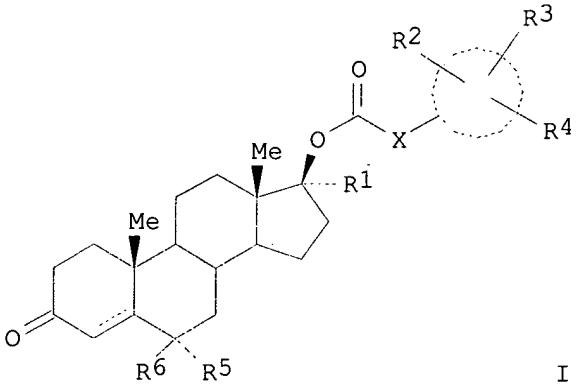


I

AB Compds. of structural formula (I) as herein defined are claimed as useful in a method for modulating a function of the androgen receptor in a tissue selective manner in a patient in need of such modulation, as well as in a method of activating the function of the androgen receptor in a patient, and in particular the method wherein the function of the androgen receptor is blocked in the prostate of a male patient or in the uterus of a female patient and activated in bone and/or muscle tissue. These compds. are useful in the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteopenia, osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, female sexual dysfunction, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, aplastic anemia and other hematopoietic disorders, pancreatic cancer, renal cancer, prostate cancer, inflammatory arthritis and joint repair, alone or in combination with other active agents. Methods for the co-administration of those compds. with bone-strengthening agents are also claimed.

L29 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:521462 CAPLUS
DOCUMENT NUMBER: 137:88442
TITLE: Incensole and furanogermacrens and compounds in treatment for inhibiting neoplastic lesions and microorganisms

INVENTOR(S): Shanahan-Pendergast, Elisabeth
PATENT ASSIGNEE(S): Ire.
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002053138 | A2 | 20020711 | WO 2002-IE1 | 20020102 |
| WO 2002053138 | A3 | 20020919 | | |
| W: AE, AG, AT, AU, BB, BG, CA, CH, CN, CO, CU, CZ, LU, LV, MA, MD, UA, UG, US, VN, YU, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, AT, BE, CH, CY, DE, ES, FI, ML, MR, NE, SN, TD, TG | | | | |
| EP 1351678 | A2 | 20031015 | EP 2002-727007 | 20020102 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| US 2004092583 | A1 | 20040513 | US 2004-250535 | 20040102 |
| PRIORITY APPLN. INFO.: | | | IE 2001-2 A | 20010102 |
| | | | WO 2002-IE1 W | 20020102 |

OTHER SOURCE(S): MARPAT 137:88442

AB The invention discloses the use of incensole and/or furanogermacrens, derivs. metabolites and precursors thereof in the treatment of neoplasia, particularly resistant neoplasia and immunodysregulatory disorders. These compds. can be administered alone or in combination with conventional chemotherapeutic, antiviral, antiparasite agents, radiation and/or surgery. Incensole and furanogermacren and their mixture showed antitumor activity against various human carcinomas and melanomas and antimicrobial activity against Staphylococcus aureus and Enterococcus faecalis.

L29 ANSWER 13 OF 13 EMBASE 
ACCESSION NUMBER: 2002390846 EMBASE
TITLE: Long-term consequences of childhood-onset congenital adrenal hyperplasia.
AUTHOR: White P.C.; Speiser P.W.
CORPORATE SOURCE: Dr. P.W. Speiser, Division of Pediatric Endocrinology, North Shore University Hospital, 300 Community Drive, Manhasset, NY 11030, United States
SOURCE: Bailliere's Best Practice and Research in Clinical Endocrinology and Metabolism, (2002) Vol. 16, No. 2, pp. 273-288. .
Refs: 81
ISSN: 1521-690X CODEN: BBPMFY
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
022 Human Genetics
007 Pediatrics and Pediatric Surgery
029 Clinical Biochemistry
030 Pharmacology
038 Adverse Reactions Titles
037 Drug Literature Index
010 Obstetrics and Gynecology
017 Public Health, Social Medicine and Epidemiology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20021114
Last Updated on STN: 20021114

AB Congenital adrenal hyperplasia (CAH) is a general term applied to several diseases caused by inherited defects of cortisol synthesis. The most common of these is steroid 21-mono-oxygenase (also termed 21-hydroxylase) deficiency (CAH-21OHD), found in approximately 1:10 000-1:15 000 live births. Potentially lethal adrenal insufficiency is characteristic of about two-thirds to three-quarters of patients with the classic salt-**wasting** form of CAH-21OHD. Non-salt-**wasting** forms of

CAH-21OHD may be diagnosed based in part on genital ambiguity in affected newborn females, and/or by later evidence of androgen excess in members of either sex. Non-classical CAH-21OHD may be detected in up to 1-3% of certain populations, and is often mistaken for idiopathic precocious pubarche in children or polycystic ovary syndrome in young women. This chapter addresses issues relating to long-term consequences in adult life of CAH-21OHD diagnosed in early childhood or adolescence.

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=> s hiv (l) wasting
L30       2303 HIV (L) WASTING

=> s hiv or human immuno virus or aids
L31     617449 HIV OR HUMAN IMMUNO VIRUS OR AIDS

=> s l31 and l2
L32         19 L31 AND L2

=> dup rem l32
PROCESSING COMPLETED FOR L32
L33         19 DUP REM L32 (0 DUPLICATES REMOVED)

=> d ibib abs 1-19

L33  ANSWER 1 OF 19  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2005:259887  CAPLUS
DOCUMENT NUMBER:          142:336518
TITLE:                    Preparation of 17β-heterocyclic-3-oxo-4-aza-
                          5α-androst-1-ene derivatives as androgen
                          receptor modulators
INVENTOR(S):              Meissner, Robert S.; Mitchell, Helen J.
PATENT ASSIGNEE(S):       Merck & Co., Inc., USA
SOURCE:                   PCT Int. Appl., 105 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2005025579         A1    20050324    WO 2004-US28641         20040902
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
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             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
PRIORITY APPLN. INFO.:                       US 2003-501664P     P  20030910
OTHER SOURCE(S):          MARPAT 142:336518
GI
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *
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AB The present invention discloses preparation of 17β-heterocyclic-3-oxo-4-aza-5α-androst-1-ene derivs., such as I [dashed bond = single bond, double bond; X = H, halo; Y, Z = H, alkyl, halo; Y and Z, together with the carbon atom to which they are attached = cyclopropyl; n = 0-3; U, V, W, D = CH, N, provided that at least U, V, W, and D = CH; R1 = H, CF3, carbonyl(alkyl), OH, alkoxy, halo, alkyl, CH2OH, alkylamino; R2 = halo, carbonyl(alkyl), carbonyl(alkenyl), carbonyl(alkynyl), alkenylamino,

heterocyclic, etc.], for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, 4-azaandrost-1-ene derivative II was reacted with 2,3-diaminopyridine in presence of silver triflate to give 17β-carboxamide derivative III, which, on heating with polyphosphoric acid, afforded 17β-imidazopyridinyl-3-oxo-4-aza-5α-androst-1-ene derivative IV. I are therefore useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, **HIV**-wasting, prostate cancer, benign prostatic hyperplasia (BPH), abdominal adiposity, metabolic syndrome, type II diabetes, cancer cachexia, Alzheimer's disease, muscular dystrophies, cognitive decline, sexual dysfunction, sleep apnea, depression, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:259881 CAPLUS
DOCUMENT NUMBER: 142:336517
TITLE: Preparation of 17-heterocyclic-4-aza-5α-androst-1-en-3-one derivatives for their use as modulators of the androgen receptor in a tissue selective manner
INVENTOR(S): Kaufman, Mildred L.; Meissner, Robert S.; Mitchell, Helen J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005025572 | A1 | 20050324 | WO 2004-US28655 | 20040902 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-501789P P 20030910
OTHER SOURCE(S): MARPAT 142:336517
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB 17-Heterocyclic-4-aza-5α-androst-1-en-3-one derivs., such as I [dashed bond = single bond, double bond; X = H, halo; Y, Z = H, alkyl, halo; Y and Z, together with the carbon atom to which they are attached = cyclopropyl; n = 0-3; U, V, W, D = CH, N, S, O; R1 = H, CF3, carbonyl(alkyl), OH, alkoxy, halo, alkyl, CH2OH, alkylamino; R2 = halo, carbonyl(alkyl), carbonyl(alkenyl), carbonyl(alkynyl), alkenylamino, heterocyclic, etc.], were prepared for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, II (R = OH)

was treated with Et3N, and iso-Bu chloroformate, followed by reaction with N,O-dimethylhydroxylamine hydrochloride to give II [R = N(Me)OMe (III)]. III was converted to 4-aza-5α-androst-1-en-3,20-dione derivative II (R = Me), and then to bromide II [R = CH2Br (IV)], which was treated with N-butyl-thiourea to afford V. The prepared compds. are useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, **HIV**-wasting, prostate cancer, benign prostatic hyperplasia (BPH), abdominal adiposity, metabolic syndrome, type II diabetes, cancer cachexia, Alzheimer's disease, muscular dystrophies, cognitive decline, sexual dysfunction, sleep apnea, depression, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:58320 CAPLUS
DOCUMENT NUMBER: 142:156210
TITLE: Preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivatives as androgen receptor modulators
INVENTOR(S): Dankulich, William P.; Kaufman, Mildred L.; Meissner, Robert S.; Mitchell, Helen J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005005606 | A2 | 20050120 | WO 2004-US20539 | 20040625 |
| WO 2005005606 | A3 | 20050602 | | |

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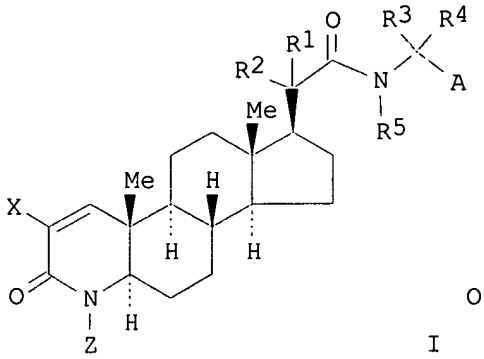
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-483675P P 20030630
OTHER SOURCE(S): MARPAT 142:156210
GI



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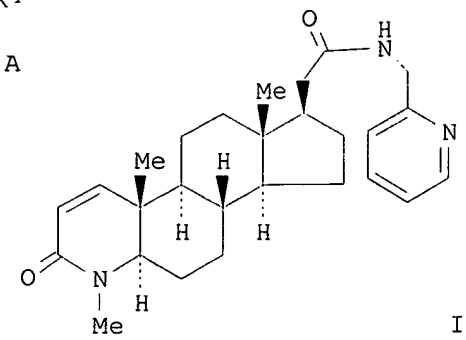


II

AB 3-Oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs., such as I [X = H, halo; Z = H, CF3, carbonylalkyl, alkyl, alkoxy, halo, CH2OH; A = aromatic ring having 0-4 heteroatoms; polycyclic ring system having one or more aromatic rings and 0-4 heteroatoms; R1, R2, R3, R4, R5 = H, halo, alkyl, amino, alkylamino, aminoalkyl, alkoxyalkyl, alkoxyalkyl, alkoxycarbonylalkyl, cyano, perfluoroalkyl, alkylcarbonyl, alkylcarbonylamino, etc.; R1R2, R3R4 = oxo, spirocycloalkyl], or a pharmaceutically acceptable salt or an enantiomer thereof, were prepared for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivative II, was prepared via a multiple step reaction sequence starting from 4-methyl-3-oxo-4-aza-5α-androst-1-ene-17-carboxylic acid and 2-aminomethylpyridine. I are therefore useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, **HIV**-wasting, prostate cancer, benign prostatic hyperplasia (BPH), cancer cachexia, Alzheimer's disease, muscular dystrophies, cognitive decline, sexual dysfunction, sleep apnea, depression, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

L33 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:55196 CAPLUS
DOCUMENT NUMBER: 142:156209
TITLE: Preparation of 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivatives as androgen receptor modulators.
INVENTOR(S): Dankulich, William P.; Kaufman, Mildred L.; Meissner, Robert S.; Mitchell, Helen J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 158 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005005380 | A2 | 20050120 | WO 2004-US20548 | 20040625 |
| WO 2005005380 | A3 | 20050602 | | |

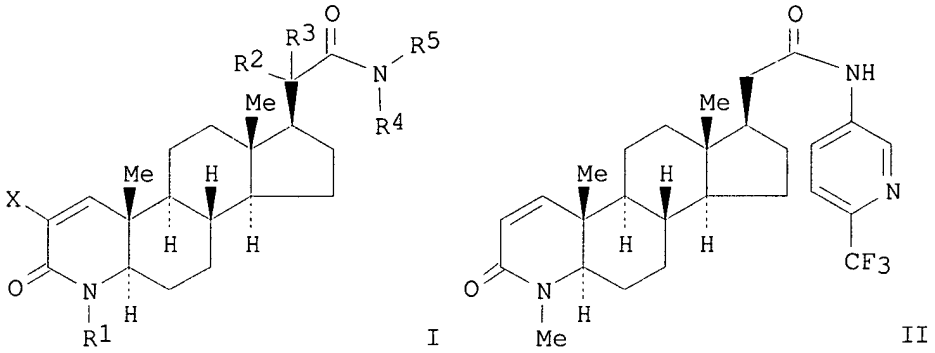
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-483784P P 20030630

OTHER SOURCE(S): MARPAT 142:156209

GI



I II

AB 3-Oxo-4-aza-5α-androst-1-ene-17β-acetamide derivs., such as I [X = H, halo; R1 = H, CF3, alkyl, alkoxy, halo, amino, alkylamino, CH2OH; R2, R3 = H, halo, alkyl, amino, aminoalkyl, alkoxyalkyl, alkoxyalkyl, alkoxycarbonylalkyl, cyano, perfluoroalkyl, alkylcarbonyl, alkylcarbonylamino; R2R3 = oxo, spirocycloalkyl; R4, R5 = H, halo, alkyl, alkenyl, alkynyl, carbonylalkyl, carbonylalkenyl, carbonylalkynyl, cycloalkyl, heterocyclyl, cycloheteroalkyl, carboxyaryl, etc.], or a pharmaceutically acceptable salt or an enantiomer thereof, were prepared for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, 3-oxo-4-aza-5α-androst-1-ene-17β-acetamide derivative II, was prepared via a multiple step reaction sequence starting from 4-methyl-3-oxo-4-aza-5α-androst-1-ene-17-carboxylic acid and 3-amino-6-trifluoromethylpyridine. The prepared compds. are useful as agonists of the androgen receptor in bone and/or muscle tissue while antagonizing the AR in the prostate of a male patient or in the uterus of a female patient. I are therefore useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, **HIV**-wasting, prostate cancer, cancer cachexia, Alzheimer's disease, muscular dystrophies, cognitive impairment, decreased libido, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

L33 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1311659 CAPLUS

DOCUMENT NUMBER: 144:51330

TITLE: N-benzyl-2-phenylbutanamides as tissue-selective androgen receptor modulators, their preparation, pharmaceutical compositions, and use in therapy

INVENTOR(S): Hanney, Barbara; Kim, Yuntae; Krout, Michael R.; Meissner, Robert S.; Mitchell, Helen J.; Musselman, Jeffrey; Perkins, James J.; Wang, Jiabing

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 50 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2005277681 | A1 | 20051215 | US 2005-145490 | 20050603 |
| WO 2005120477 | A2 | 20051222 | WO 2005-US19554 | 20050603 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-577698P P 20040607

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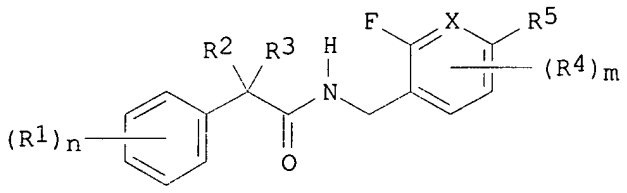


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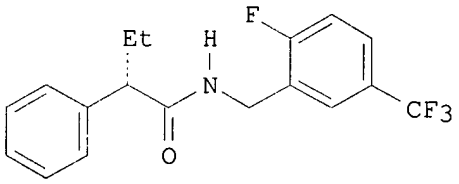


II

AB The invention relates to compds. of structural formula I, which are modulators of the androgen receptor (AR) in a tissue-selective manner. In compds. I, X is CH or N; n is 0, 1, 2, or 3; m is 0, 1, or 2; R1, R4, and R5 are independently selected from H, halo, cyano, (un)substituted C1-10 alkyl, (un)substituted C2-10 alkenyl, (un)substituted aryl-C0-10 alkyl, (un)substituted perfluoro-C1-6 alkyl, etc.; R2 and R3 are independently selected from H, halo, cyano, amino, hydroxy-C0-10 alkyl, (un)substituted C1-10 alkyl, (un)substituted C2-10 alkenyl, (un)substituted aryl-C0-10 alkyl, (un)substituted perfluoro-C1-6 alkyl, etc. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of a compound I and a pharmaceutically acceptable carrier, as well as to the use of the compns. for the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration. Coupling of (S)-2-phenylbutanoic acid with 2-fluoro-5-(trifluoromethyl)benzylamine gave butanamide II. Compds. of the invention, e.g., II, express affinity for endogenously expressed androgen receptor with IC50 values of 1 μM or less.

L33 ANSWER 6 OF 19 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:509262 BIOSIS
DOCUMENT NUMBER: PREV200510298998
TITLE: International Congress Series.
AUTHOR(S): Slager, E [Editor]; Fauser, B [Editor]; VanGeijn, H [Editor]; Brolmann, H [Editor]; Vervest, H [Editor]
SOURCE: Slager, E [Editor]; Fauser, B [Editor]; VanGeijn, H [Editor]; Brolmann, H [Editor]; Vervest, H [Editor]. Int. Congr. Ser. - Excerpta Med., (2005) International Congress

Series.
Publisher: ELSEVIER SCIENCE BV, SARA BURGERHARTSTRAAT 25, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS. Series: INTERNATIONAL CONGRESS SERIES.
CODEN: EXMDA4. ISSN: 0531-5131. ISBN: 0-444-51917-3(H).
DOCUMENT TYPE: Book
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Nov 2005
Last Updated on STN: 23 Nov 2005

AB This 476-page book, which is based on the proceedings of the Fifteenth Congress of Gynecology, Obstetrics and Reproductive Medicine, is volume 1279 of the International Congress Series and this volume focuses on gynecology, obstetricsand reproductive medicine in daily practice. The congress was held in Rotterdam, The Netherlands, in April 2005. The book is structured into 5 major sections, which in turn may be divided into more specific sections. There are 71 individually-authored papers in total, which include key note lectures. The text is in English and all of the papers are extensively-referenced. Fertility research and treatment in 2005 is the focus of the first section, which contains 11 papers, and topics discussed in the more specific subsections include anovulation diagnostics, ovulation induction, ovarian stimulation, and intrauterine insemination. Gynecology is the focus of the next major section and is discussed in terms of disease prevention, diagnostics and therapy in 2005. Specific subsections within this second section deal with chronic pelvic pain, infections, endometrial carcinoma, and new diagnostics and operating techniques. The third major section deals with postgraduate course prenatal imaging and screening and specific areas outlined include the mid-gestational scan, ultrasound examination in twin pregnancies, nuchal translucency, first trimester ultrasound screening for chromosomal anomalies, a national screening program for Downs syndrome and neural tube defects in the Netherlands, Down syndrome screening, fetal aneuploidy screening practice in Flanders and Belgium, and prenatal screening and the communication and perception of risks. The next major section overviews obstetrics with respect to preconceptional, antenatal and perinatal prevention of morbidity and mortality in 2005, and more specific subsections discuss preconceptional counselling, antepartum fetal care, intrapartum fetal care,postpartum hemorrhage, and newborn life support. The final major section discusses postgraduate course vaginal prolapse and urine incontinence. The book isindexed by author and by keyword. This book will be of interest to gynecologists, urologists, obstetricians and anyone interested in reproductive medicine.

L33 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:1015853 CAPLUS
DOCUMENT NUMBER: 142:1359
TITLE: Identification and synthesis of androgen receptor modulators and therapeutic uses thereof
INVENTOR(S): Meissner, Robert S.; Perkins, James J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 165 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004100874 | A2 | 20041125 | WO 2004-US13787 | 20040503 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,

SN, TD, TG

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|---|---|---|---|---|
| CA 2524409 | AA | 20041125 | CA 2004-2524409 | 20040503 |
| EP 1622567 | A2 | 20060208 | EP 2004-751257 | 20040503 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR

PRIORITY APPLN. INFO.: US 2003-468579P P 20030507
WO 2004-US13787 W 20040503

OTHER SOURCE(S): MARPAT 142:1359

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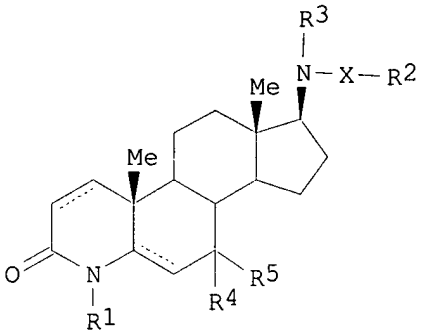

I

AB Compds. of structural formula (I) as herein defined are disclosed as useful in a method for modulating the androgen receptor in a tissue selective manner in a patient in need of such modulation, as well as in a method of agonizing the androgen receptor in a patient, and in particular the method wherein the androgen receptor is antagonized in the prostate of a male patient or in the uterus of a female patient and agonized in bone and/or muscle tissue. Method for the synthesis of those compds., as well as techniques for the screening of androgen receptor modulation capacity of those compds. are exemplified. These compds. are useful in the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including: osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, post-menopausal symptoms in women, female sexual dysfunction, atherosclerosis, hypercholesterolemia, hyperlipidemia, aplastic anemia and other hematopoietic disorders, pancreatic cancer, renal cancer, arthritis and joint repair, alone or in combination with other active agents. In addition, these compds. are useful as pharmaceutical composition ingredients alone and in combination with other active agents.

L33 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:412812 CAPLUS
DOCUMENT NUMBER: 140:406808
TITLE: Preparation of carbonylamino-benzimidazoles as selective androgen receptor modulators
INVENTOR(S): Kim, Yuntae; Spencer, Keith L.; Hanney, Barbara; Duggan, Mark E.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 136 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004041277 | A1 | 20040521 | WO 2003-US34345 | 20031028 |

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TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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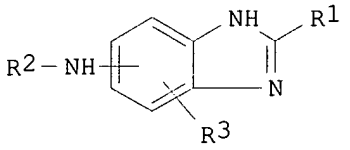
|---|---|---|---|---|---|
| CA 2504044 | AA | 20040521 | CA 2003-2504044 | | 20031028 |
| EP 1581217 | A1 | 20051005 | EP 2003-777969 | | 20031028 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | | |
| US 2006036098 | A1 | 20060216 | US 2005-533259 | | 20050429 |
| PRIORITY APPLN. INFO.: | | | US 2002-422914P | P | 20021101 |
| | | | WO 2003-US34345 | W | 20031028 |

OTHER SOURCE(S): MARPAT 140:406808
GI

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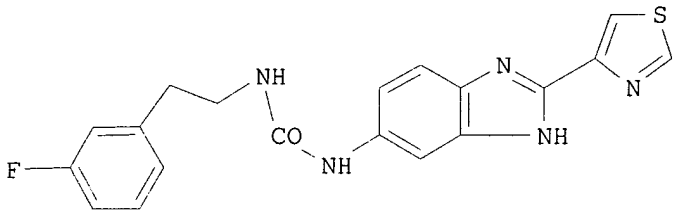



II

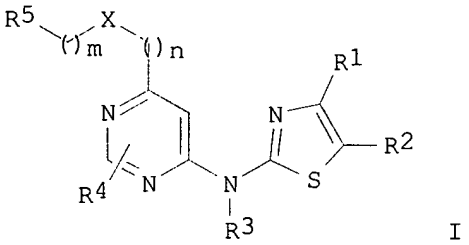
AB Carbonylamino-benzimidazoles (shown as I; variables defined below; e.g. II) are modulators of the androgen receptor (AR) in a tissue selective manner. They are useful as agonists of the androgen receptor in bone and/or muscle tissue while antagonizing the AR in the prostate of a male patient or in the uterus of a female patient. These compds. are therefore useful in the enhancement of weakened muscle tone and the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, arthritic condition and joint repair, **HIV**-wasting, prostate cancer, cancer cachexia, Alzheimer's disease, muscular dystrophies, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents. Although the methods of preparation are not claimed, 6 example prepns. and characterization data for .apprx.150 examples of I are included; nearly all examples contain the thiazol-4-yl group at the 2 position of the benzimidazole. For example, II was prepared from 3-fluorophenethylamine, 1,1'-carbonyldiimidazole and [2-(thiazol-4-yl)-3H-benzimidazol-5-yl]amine, the latter of which was prepared from thiazole-4-carboxylic acid and (4-amino-3-nitrophenyl)carbamic acid tert-Bu ester (preparation described) via amide formation followed by cyclization in 20% aqueous AcOH. For I: R1 = aryl or heterocyclyl; R2 = -(C:O)NR5R6, -(C:O)a(C1-10)alkyl, -(C:O)a(C2-8)alkenyl, -(C:O)a(C2-8)alkynyl, -(C:O)a(C3-10)cycloalkyl, -(C:O)a(C3-8)heterocyclyl, and -(C:O)aaryl; R3 = H, halogen, -(C:O)aOb(C1-10)alkyl, -(C:O)aOb(C2-8)alkenyl, -(C:O)aOb(C2-8)alkynyl, -(C:O)aOb(C3-10)cycloalkyl, -(C:O)aOb(C3-8)heterocyclyl, -(C:O)aObaryl, -(C:O)aNR5R6, -Ob(C:O)NR5R6, -NR5(C:O)aObRb, -NR5(C:O)NR5R6, -NR5S(O)2Rb, -(C:O)OH, trifluoromethoxy, trifluoroethoxy, -Ob(C1-10)perfluoroalkyl, -S(O)2Ob(C1-10)alkyl, -S(O)2Ob(C2-8)alkenyl, -S(O)2Ob(C2-8)alkynyl, -S(O)2Ob(C3-10)cycloalkyl, -S(O)2Ob(C3-8)heterocyclyl, -S(O)2Obaryl, -NR5S(O)2NR5R6, -CN, -NO2, oxo, and -OH; a = 0-1; b = 0-1; addnl. details are given in the claims.

L33 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:412750 CAPLUS
DOCUMENT NUMBER: 140:423687
TITLE: Preparation of thiazolylamino-substituted pyrimidines as kinase inhibitors
INVENTOR(S): Hartman, George D.; Hoffman, Jacob M.; Smith, Anthony M.; Tucker, Thomas J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

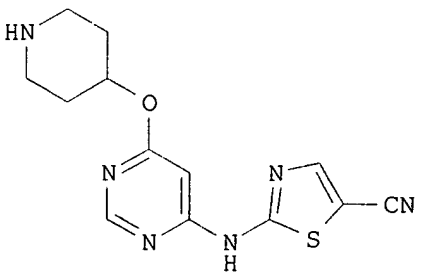
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004041164 | A2 | 20040521 | WO 2003-US34100 | 20031024 |
| WO 2004041164 | A3 | 20041007 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2503715 | AA | 20040521 | CA 2003-2503715 | 20031024 |
| EP 1558609 | A2 | 20050803 | EP 2003-779322 | 20031024 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |

PRIORITY APPLN. INFO.: US 2002-422313P P 20021030
WO 2003-US34100 W 20031024

OTHER SOURCE(S): MARPAT 140:423687
GI




I




II

AB Title compds. I [X = O, S, amino; m,n = 0-3; R1-2, R4 = H, OH, alkoxy, CN,

etc.; R3 = H, sulfonyl, acyl, carboxy, etc.; R5 = heterocyclyl] are prepared For instance, tert-Bu 4-[(6-aminopyrimidin-4-yl)oxy]piperidine-1-carboxylate (preparation given) is reacted with 2-chlorothiazole-5-carbonitrile (THF, NaH) and the resulting product deprotected (CH2Cl2, TFA) to give II. I inhibit, regulate and/or modulate kinase signal transduction; they are useful in the treatment of kinase-dependent diseases and conditions, such as angiogenesis, cancer, tumor growth, atherosclerosis, age related macular degeneration, retinal ischemia, macular edema, diabetic retinopathy and inflammatory diseases.

L33 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:722925 CAPLUS
DOCUMENT NUMBER: 141:218967
TITLE: Methods and compositions with **trans-clomiphene** for treating wasting and lipodystrophy
INVENTOR(S): Podolski, Joseph S.; Wiehle, Ronald
PATENT ASSIGNEE(S): Zonagen, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 12 pp., Cont.-in-part of U.S. Ser. No. 427,768.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2004171697 | A1 | 20040902 | US 2003-712546 | 20031112 |
| WO 2003005954 | A2 | 20030123 | WO 2002-US21524 | 20020709 |
| WO 2003005954 | A3 | 20031023 | | |
| WO 2003005954 | B1 | 20031204 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2004097597 | A1 | 20040520 | US 2003-427768 | 20030430 |

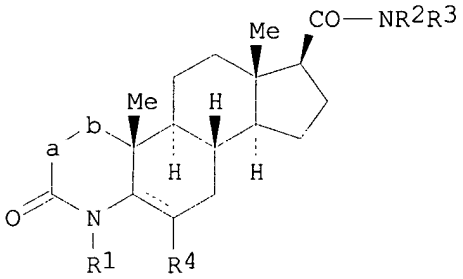
PRIORITY APPLN. INFO.:
US 2001-304313P P 20010709
WO 2002-US21524 A2 20020709
US 2003-427768 A2 20030430

AB The invention discloses compns. and methods useful for treating wasting, especially a loss of muscle mass. The present invention also discloses compns. and methods useful for treating lipodystrophy. The compns. and methods of the present invention are particularly beneficial to **HIV** -infected individuals.

L33 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:892539 CAPLUS
DOCUMENT NUMBER: 139:375605
TITLE: Synthesis and uses of 4-azasteroid derivatives as selective androgen receptor modulators (SARMs)
INVENTOR(S): Wang, Jiabing; McVean, Carol A.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 181 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003092588 | A2 | 20031113 | WO 2003-US13120 | 20030425 |

WO 2003092588 A3 20040715
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
CA 2484173 AA 20031113 CA 2003-2484173 20030425
EP 1501512 A2 20050202 EP 2003-719957 20030425
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
US 2005131005 A1 20050616 US 2003-512800 20030425
JP 2005529897 T2 20051006 JP 2004-500773 20030425
PRIORITY APPLN. INFO.: US 2002-376779P P 20020430
WO 2003-US13120 W 20030425
OTHER SOURCE(S): MARPAT 139:375605
GI



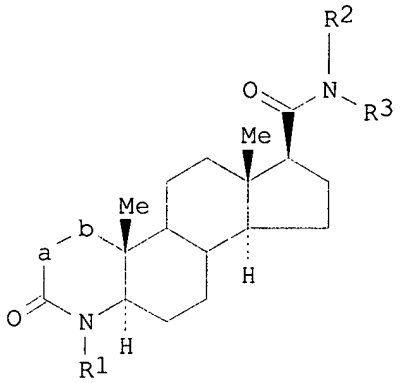

AB Compds. of structural formula (I) are modulators of the androgen receptor (AR) in a tissue selective manner. They are useful as agonists of the androgen receptor in bone and/or muscle tissue while antagonizing the AR in the prostate of a male patient or in the uterus of a female patient. These compds. are therefore useful in the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, **HIV**-wasting, prostate cancer, cancer cachexia, Alzheimer's disease, muscular dystrophies, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

L33 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:757525 CAPLUS
DOCUMENT NUMBER: 139:277056
TITLE: Preparation of fluorinated 4-aza-androstan-3-one-17β-carboxamide derivatives as androgen receptor modulators
INVENTOR(S): Meissner, Robert S.; Perkins, James J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

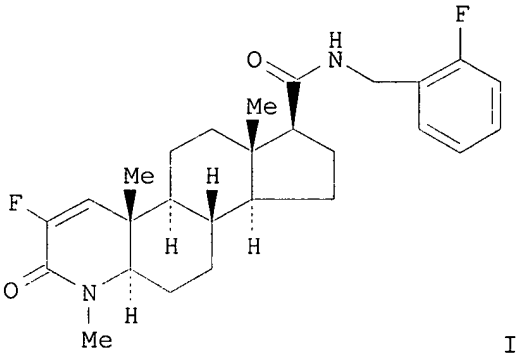
| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 2003077919 | A1 | 20030925 | WO 2003-US8277 | | 20030307 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | | |
| CA 2478186 | AA | 20030925 | CA 2003-2478186 | | 20030307 |
| AU 2003218235 | A1 | 20030929 | AU 2003-218235 | | 20030307 |
| EP 1485095 | A1 | 20041215 | EP 2003-714228 | | 20030307 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, SK | | | | | |
| BR 2003008355 | A | 20050125 | BR 2003-8355 | | 20030307 |
| US 2005165039 | A1 | 20050728 | US 2003-507239 | | 20030307 |
| JP 2005526082 | T2 | 20050902 | JP 2003-575972 | | 20030307 |
| NO 2004004312 | A | 20041012 | NO 2004-4312 | | 20041012 |
| PRIORITY APPLN. INFO.: | | | US 2002-363822P | P | 20020313 |
| | | | WO 2003-US8277 | W | 20030307 |

OTHER SOURCE(S): MARPAT 139:277056

GI




I




II

AB Fluorinated 4-aza-androstan-3-one-17β-carboxamide derivs., such as I [a-b = CF:CH, CHFCH2, CF2CH2; R1 = H, CH2OH, (un)substituted alkyl; R2 = H, alkyl; R3 = alkyl, cycloheteroalkyl, aryl, heteroaryl; R2R3 = 5 or 6-membered ring fused with a 5- or 6-membered aromatic ring system having 0-2 heteroatoms], or a pharmaceutically acceptable salt or an enantiomer thereof, were prepared for their use as modulators of the androgen receptor (AR) in a tissue selective manner. Thus, 4-aza-androstan-3-one-17β-carboxamide derivative II, was prepared via a multiple step reaction sequence starting from 4-methyl-4-aza-androstan-3-one-17-carboxylic acid Me ester and 2-fluoro-benzylamine. The prepared compds. are useful as agonists of the androgen receptor in bone and/or muscle tissue while antagonizing the AR in the prostate of a male patient or in the uterus of a female patient. I are therefore useful in the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteoporosis, osteopenia, glucocorticoid-induced osteoporosis, periodontal disease, bone fracture, bone damage following bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, obesity, aplastic anemia and other hematopoietic disorders, inflammatory arthritis and joint repair, **HIV**-wasting, prostate cancer, cancer cachexia, muscular dystrophies, premature ovarian failure, and autoimmune disease, alone or in combination with other active agents.

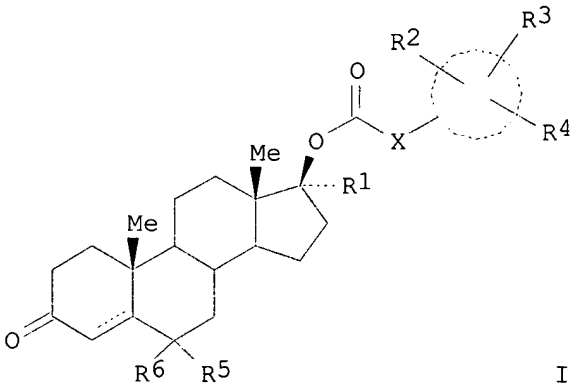
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

L33 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:261603 CAPLUS
DOCUMENT NUMBER: 138:281598
TITLE: Androstane compounds as androgen receptor (AR) modulators for the treatment of AR-related diseases
INVENTOR(S): Wang, Jiabing
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003026568 | A2 | 20030403 | WO 2002-US29436 | 20020917 |
| WO 2003026568 | A3 | 20040226 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2459943 | AA | 20030403 | CA 2002-2459943 | 20020917 |
| EP 1429779 | A2 | 20040623 | EP 2002-766288 | 20020917 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| JP 2005507886 | T2 | 20050324 | JP 2003-530207 | 20020917 |
| US 2004235808 | A1 | 20041125 | US 2004-489072 | 20040308 |

PRIORITY APPLN. INFO.: US 2001-324124P P 20010921
WO 2002-US29436 W 20020917

OTHER SOURCE(S): MARPAT 138:281598
GI




I

AB Compds. of structural formula (I) as herein defined are claimed as useful in a method for modulating a function of the androgen receptor in a tissue selective manner in a patient in need of such modulation, as well as in a method of activating the function of the androgen receptor in a patient, and in particular the method wherein the function of the androgen receptor is blocked in the prostate of a male patient or in the uterus of a female patient and activated in bone and/or muscle tissue. These compds. are useful in the treatment of conditions caused by androgen deficiency or which can be ameliorated by androgen administration, including osteopenia, osteoporosis, periodontal disease, bone fracture, bone damage following

bone reconstructive surgery, sarcopenia, frailty, aging skin, male hypogonadism, female sexual dysfunction, postmenopausal symptoms in women, atherosclerosis, hypercholesterolemia, hyperlipidemia, aplastic anemia and other hematopoietic disorders, pancreatic cancer, renal cancer, prostate cancer, inflammatory arthritis and joint repair, alone or in combination with other active agents. Methods for the co-administration of those compds. with bone-strengthening agents are also claimed.

L33 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:521462 CAPLUS
DOCUMENT NUMBER: 137:88442
TITLE: Incensole and furanogermacrens and compounds in treatment for inhibiting neoplastic lesions and microorganisms
INVENTOR(S): Shanahan-Pendergast, Elisabeth
PATENT ASSIGNEE(S): Ire.
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002053138 | A2 | 20020711 | WO 2002-IE1 | 20020102 |
| WO 2002053138 | A3 | 20020919 | | |
| W: AE, AG, AT, AU, BB, BG, CA, CH, CN, CO, CU, CZ, LU, LV, MA, MD, UA, UG, US, VN, YU, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, AT, BE, CH, CY, DE, ES, FI, ML, MR, NE, SN, TD, TG | | | | |
| EP 1351678 | A2 | 20031015 | EP 2002-727007 | 20020102 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| US 2004092583 | A1 | 20040513 | US 2004-250535 | 20040102 |
| PRIORITY APPLN. INFO.: | | | IE 2001-2 A | 20010102 |
| | | | WO 2002-IE1 W | 20020102 |

OTHER SOURCE(S): MARPAT 137:88442
AB The invention discloses the use of incensole and/or furanogermacrens, derivs. metabolites and precursors thereof in the treatment of neoplasia, particularly resistant neoplasia and immunodysregulatory disorders. These compds. can be administered alone or in combination with conventional chemotherapeutic, antiviral, antiparasite agents, radiation and/or surgery. Incensole and furanogermacren and their mixture showed antitumor activity against various human carcinomas and melanomas and antimicrobial activity against Staphylococcus aureus and Enterococcus faecalis.

L33 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:293427 CAPLUS
DOCUMENT NUMBER: 129:8597
TITLE: Embedding and encapsulation of controlled release particles
INVENTOR(S): Van Lengerich, Bernhard H.
PATENT ASSIGNEE(S): Van Lengerich, Bernhard H., USA
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9818610 | A1 | 19980507 | WO 1997-US18984 | 19971027 |
| W: AU, CA, JP, NO, PL, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| CA 2269806 | AA | 19980507 | CA 1997-2269806 | 19971027 |
| CA 2269806 | C | 20060124 | | |
| AU 9749915 | A1 | 19980522 | AU 1997-49915 | 19971027 |

| | | | | |
|---|---|---|---|---|
| AU 744156 | B2 | 20020214 | | |
| EP 935523 | A1 | 19990818 | EP 1997-912825 | 19971027 |
| EP 935523 | B1 | 20040929 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2002511777 | T2 | 20020416 | JP 1998-520558 | 19971027 |
| EP 1342548 | A1 | 20030910 | EP 2003-10031 | 19971027 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| AT 277739 | E | 20041015 | AT 1997-912825 | 19971027 |
| NO 9902036 | A | 19990428 | NO 1999-2036 | 19990428 |
| PRIORITY APPLN. INFO.: | | | US 1996-29038P | P 19961028 |
| | | | US 1997-52717P | P 19970716 |
| | | | EP 1997-912825 | A3 19971027 |
| | | | WO 1997-US18984 | W 19971027 |

AB Controlled release, discrete, solid particles which contain an encapsulated and/or embedded component such as a heat sensitive or readily oxidizable pharmaceutically, biol., or nutritionally active component are continuously produced without substantial destruction of the matrix material or encapsulant. A release-rate controlling component is incorporated into the matrix to control the rate of release of the encapsulant from the particles. The addnl. component may be a hydrophobic component or a high water binding capacity component for extending the release time. The plasticizable matrix material, such as starch, is admixed with at least one plasticizer, such as water, and at least one release-rate controlling component under low shear mixing conditions to plasticize the plasticizable material without substantially destroying the at least one plasticizable material and to obtain a substantially homogeneous plasticized mass. The plasticizer content is substantially reduced and the temperature of the plasticized mass is substantially reduced prior to admixing the plasticized mass with the encapsulant to avoid substantial destruction of the encapsulant and to obtain a formable, extrudable mixture The mixture is extruded though a die without substantial or essentially no expansion and cut into discrete, relatively dense particles. Release properties may also be controlled by precoating the encapsulant and/or coating the extruded particles with a film-forming component. An example of encapsulation of acetylcysteine is given using starch, polyethylene, glycerol monostearate, and vegetable oil.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 16 OF 19 EMBASE 

ACCESSION NUMBER: 1998421746 EMBASE
TITLE: Reproductive effects of nontesticular illness.
AUTHOR: Baker H.W.G.
CORPORATE SOURCE: Dr. H.W.G. Baker, University of Melbourne, Dept. of Obstetrics and Gynaecology, Royal Women's Hospital, Carlton, Vic. 3058, Australia
SOURCE: Endocrinology and Metabolism Clinics of North America, (1998) Vol. 27, No. 4, pp. 831-850. .
Refs: 96
ISSN: 0889-8529 CODEN: ECNAER
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
010 Obstetrics and Gynecology
028 Urology and Nephrology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19990128
Last Updated on STN: 19990128

AB Diseases in other organs may impair the male reproductive system. Acute critical conditions such as severe trauma, surgery, myocardial infarction, burns, liver failure, intoxication, or starvation are associated with suppression of gonadotropin secretion and secondary hypogonadism. With chronic illnesses, a primary testicular disorder with elevated

gonadotropin levels may occur. This may be associated with increased peripheral conversion of androgens to estrogens, resulting in clinical presentation of combined androgen deficiency and estrogen excess. The association of hypogonadism and feminization with cirrhosis of the liver is a classic example. Types of hypogonadism that may occur with chronic anemia, chronic renal failure, chronic spinal cord injury, thyroid diseases, Cushing's syndrome, diabetes mellitus, obesity, **HIV** infection, neoplasia, and other chronic illnesses are also described. Numerous drugs have side effects on the reproductive system.

L33 ANSWER 17 OF 19 MEDLINE on STN
ACCESSION NUMBER: 91300152 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2070114
TITLE: Infertility management in **HIV** positive couples: a dilemma.
AUTHOR: Smith J R; Forster G E; Kitchen V S; Hooi Y S; Munday P E; Paintin D B
CORPORATE SOURCE: St Mary's Hospital, London.
SOURCE: BMJ (Clinical research ed.), (1991 Jun 15) Vol. 302, No. 6790, pp. 1447-50.
Journal code: 8900488. ISSN: 0959-8138.
Report No.: KIE-33645.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Bioethics; Priority Journals; AIDS
ENTRY MONTH: 199108
ENTRY DATE: Entered STN: 19910908
Last Updated on STN: 20030318
Entered Medline: 19910822

L33 ANSWER 18 OF 19 MEDLINE on STN
ACCESSION NUMBER: 91020580 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2219439
TITLE: Infertility: an approach to management in a district hospital in Ghana.
AUTHOR: Fiander A
CORPORATE SOURCE: Bawku Hospital, Upper East Region, Ghana.
SOURCE: Tropical doctor, (1990 Jul) Vol. 20, No. 3, pp. 98-100.
Journal code: 1301706. ISSN: 0049-4755.
Report No.: CPFH-27180cr990; POP-00195546.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Population
ENTRY MONTH: 199011
ENTRY DATE: Entered STN: 19910117
Last Updated on STN: 20021101
Entered Medline: 19901116

AB Up to 1/3 of women of child bearing age are infertile in certain African areas. Over 1000 patients registered at Bawku Hospital, Upper East Region, Ghana during an 18-month period, where a scheme for the investigation and treatment of infertile patients was established. The 5 main causes of infertility are: 1) tubal damage; 2) male factor; 3) anovulation; 4) uterine factor; and 5) unexplained. Special clinics are set up for infertility; outpatient staff are recruited. A preprinted questionnaire should be used for a uniform approach. The one used in Bawku is shown in the appendix. Health talks should be given. They should use the local language be at the right level, and use visual **aids**. In large clinics, numbers should be used to insure a 1st come, 1st served basis. A treatment protocol is important. When the patient 1st walks in, the infertility form is completed; appropriate investigations are done--hemoglobin, VDRL, seminal analysis, and cervical or high vagina swabs, and others--and the results are reviewed. The patient is encouraged to keep a menstrual calendar for 3 months. At the 2nd visit, the menstrual calendar is reviewed. A pelvic examination and a tubal patency test (TPT) are done. At the 3rd visit, abdominal and pelvic

examinations are done and a TPT. Then patients can be diagnosed and counselled accordingly. At the last visit, further explanation is given, further TPTs are done if necessary, and anovulation is treated with **clomiphene**. The visits are spread out over 6 months. In unexplained fertility cases, the couple is told there is nothing wrong, they should keep trying. The idea that the man may be causing the infertility is foreign to many communities. This needs changing. 20% of infertility is due to male factor in Bawku. Male infertility is hard to cure. Cultural considerations prevent the clinician from telling the patient that her partner is infertile. They will tell her that there is nothing wrong with her. Approximately 15% become pregnant. The clinic has a strong psychological component.

L33 ANSWER 19 OF 19 EMBASE 

ACCESSION NUMBER: 86059646 EMBASE
DOCUMENT NUMBER: 1986059646
TITLE: Abdominal pregnancy following gonadotropin treatment.
AUTHOR: Saracoglu F.O.; Goksin E.; Durukan T.
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Hacettepe University School of Medicine, Ankara, Turkey
SOURCE: American Journal of Obstetrics and Gynecology, (1985) Vol. 153, No. 7, pp. 804-805. .
CODEN: AJOGAH
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
010 Obstetrics and Gynecology
003 Endocrinology
LANGUAGE: English
ENTRY DATE: Entered STN: 911210
Last Updated on STN: 911210

AB An abdominal pregnancy after treatment with human menopausal and chorionic gonadotropins is reported. The role of induction of ovulation with human menopausal and chorionic gonadotropins as a cause of ectopic pregnancy has not been delineated. However, it appears that ultrasonography has become one of the most important **aids** in the diagnosis of abdominal pregnancy.

L33 ANSWER 16 OF 19 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1998421746 EMBASE
TITLE: Reproductive effects of nontesticular illness.
AUTHOR: Baker H.W.G.
CORPORATE SOURCE: Dr. H.W.G. Baker, University of Melbourne, Dept. of Obstetrics and Gynaecology, Royal Women's Hospital, Carlton, Vic. 3058, Australia
SOURCE: Endocrinology and Metabolism Clinics of North America, (1998) Vol. 27, No. 4, pp. 831-850. .
Refs: 96
ISSN: 0889-8529 CODEN: ECNAER
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
010 Obstetrics and Gynecology
028 Urology and Nephrology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19990128
Last Updated on STN: 19990128

AB Diseases in other organs may impair the male reproductive system. Acute critical conditions such as severe trauma, surgery, myocardial infarction, burns, liver failure, intoxication, or starvation are associated with suppression of gonadotropin secretion and secondary hypogonadism. With chronic illnesses, a primary testicular disorder with elevated gonadotropin levels may occur. This may be associated with increased peripheral conversion of androgens to estrogens, resulting in clinical presentation of combined androgen deficiency and estrogen excess. The association of hypogonadism and feminization with cirrhosis of the liver is a classic example. Types of hypogonadism that may occur with chronic anemia, chronic renal failure, chronic spinal cord injury, thyroid diseases, Cushing's syndrome, diabetes mellitus, obesity, **HIV** infection, neoplasia, and other chronic illnesses are also described. Numerous drugs have side effects on the reproductive system.

L33 ANSWER 17 OF 19 MEDLINE on STN

ACCESSION NUMBER: 91300152 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2070114
TITLE: Infertility management in **HIV** positive couples: a dilemma.
AUTHOR: Smith J R; Forster G E; Kitchen V S; Hooi Y S; Munday P E; Paintin D B
CORPORATE SOURCE: St Mary's Hospital, London.
SOURCE: BMJ (Clinical research ed.), (1991 Jun 15) Vol. 302, No. 6790, pp. 1447-50.
Journal code: 8900488. ISSN: 0959-8138.
Report No.: KIE-33645.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Bioethics; Priority Journals; AIDS
ENTRY MONTH: 199108
ENTRY DATE: Entered STN: 19910908
Last Updated on STN: 20030318
Entered Medline: 19910822

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| NEWS 5 | DEC 14 | 2006 MeSH terms loaded for MEDLINE file segment of TOXCENTER |
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| NEWS 8 | DEC 23 | New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/ USPAT2 |
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| NEWS 18 | FEB 22 | Updates in EPFULL; IPC 8 enhancements added |
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